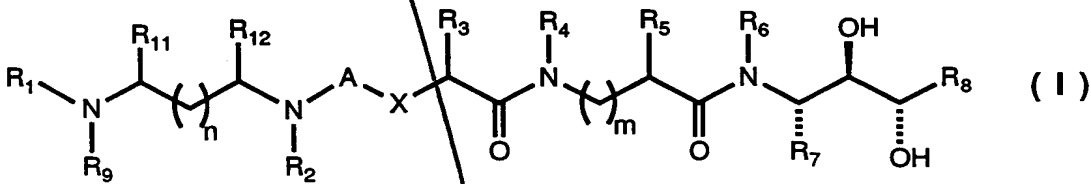
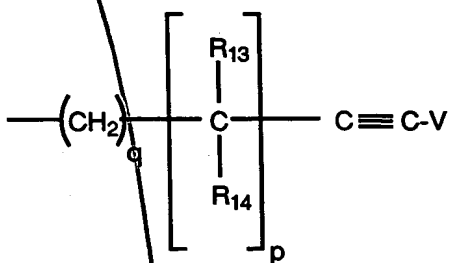


What Is Claimed Is:

1. A compound of Formula I:



wherein A is selected from methylene, CO, SO and SO₂;
wherein X is selected from oxygen atom, methylene and
NR₁₀ with R₁₀ selected from hydrido, alkyl and benzyl;
wherein each of R₁ and R₉ is a group independently
selected from hydrido, alkyl, cycloalkyl, alkoxyacyl,
haloalkyl, alkoxycarbonyl, benzyloxycarbonyl,
loweralkanoyl, haloalkylacyl, phenyl, benzyl, naphthyl,
and naphthylmethyl, any one of which groups having a
substitutable position may be optionally substituted with
one or more radicals selected from alkyl, alkoxy, alkenyl,
alkynyl, halo, haloalkyl, cyano and phenyl, and wherein
the nitrogen atom to which R₁ and R₉ are attached may be
combined with oxygen to form an N-oxide; wherein R₂ is
selected from hydrido, alkyl, dialkylaminoalkyl,
alkylacylaminoalkyl, benzyl and cycloalkyl; wherein R₃ is
selected from alkyl, cycloalkylalkyl, acylaminoalkyl,
phenylalkyl, naphthylmethyl, aryl, heterocyclicalkyl and
heterocycliccycloalkyl, wherein the cyclic portion of any
of said phenylalkyl, naphthylmethyl, aryl,
heterocyclicalkyl and heterocycliccycloalkyl groups may be
substituted by one or more radicals selected from halo,
hydroxy, alkoxy and alkyl; wherein each of R₄ and R₆ is
independently selected from hydrido, alkyl, benzyl and
cycloalkyl; wherein each of R₅ and R₈ is independently
selected from



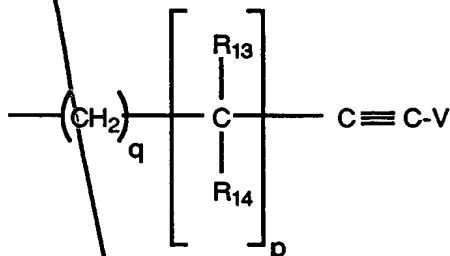
wherein V is selected from hydrido, alkyl, cycloalkyl, haloalkyl, benzyl and phenyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, phenyl, heterocyclic, heterocyclicalkyl and heterocycliccycloalkyl; wherein R₇ is selected from substituted or unsubstituted alkyl, cycloalkyl, phenyl, cycloalkylalkyl and phenylalkyl, any one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo, haloalkyl, alkenyl, alkynyl and cyano; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, haloalkyl, dialkylamino and phenyl; and wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

20

2. Compound of Claim 1 wherein A is selected from methylene, CO, SO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido, alkyl and benzyl; wherein each of R₁ and R₉ is independently selected from hydrido, lower alkyl, haloalkyl, cycloalkyl, alkoxycarbonyl, benzyloxycarbonyl, loweralkanoyl, alkoxyacyl, phenyl and benzyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein each of R₂, R₄ and R₆ is independently selected from hydrido and alkyl; wherein R₃ is selected from phenylalkyl, naphthylmethyl, cyclohexylalkyl, cyclopentylalkyl,

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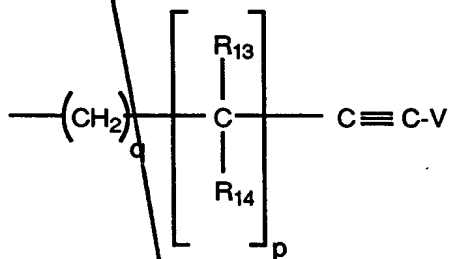
heteroarylalkyl and heteroarylcycloalkyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl, haloalkyl, benzyl and phenyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, heteroarylalkyl and heteroarylcycloalkyl; wherein R₇ is selected from substituted or unsubstituted cyclohexylmethyl and benzyl, either one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo and haloalkyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

3. Compound of Claim 2 wherein A is selected from methylene, CO, SO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido, alkyl and benzyl; wherein each of R₁ and R₉ is independently selected from hydrido, alkyl, alkoxyacyl, haloalkyl, alkoxy carbonyl, benzyloxycarbonyl and benzyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein each of R₂, R₄ and R₆ is independently selected from hydrido and alkyl; wherein R₃ is selected from benzyl, phenethyl, cyclohexylmethyl, phenpropyl, pyrrolidinyl, piperidinyl, pyrrolidinylmethyl,

piperidinylmethyl, pyrazolemethyl, pyrazoleethyl,
pyridylmethyl, pyridylethyl, thiazolemethyl,
thiazoleethyl, imidazolemethyl, imidazoleethyl,
thienylmethyl, thienylethyl, furanylmethyl, furanylethyl,
5 oxazolemethyl, oxazoleethyl, isoxazolemethyl,
isoxazoleethyl, pyridazinemethyl, pyridazineethyl,
pyrazinemethyl and pyrazineethyl; wherein each of R₅ and
R₈ is independently selected from



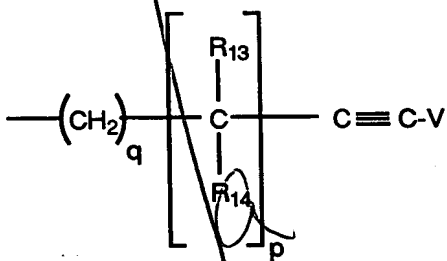
wherein V is selected from hydrido, alkyl and haloalkyl;
wherein each of R₁₃ and R₁₄ is a radical independently
selected from hydrido, alkyl, alkenyl, alkynyl, thiazole
and thiazolemethyl; wherein R₇ is cyclohexylmethyl;
wherein each of R₁₁ and R₁₂ is independently selected
from hydrido, alkyl, dialkylamino and phenyl; wherein m
is zero or one; wherein n is a number selected from zero
through five; wherein p is a number selected from zero
20 through five; and wherein q is a number selected from
zero through five; or a pharmaceutically-acceptable salt
thereof.

4. Compound of Claim 3 wherein A is selected
25 from CO and SO₂; wherein X is selected from oxygen atom,
methylene and >NR_{10} with R₁₀ selected from hydrido and
methyl; wherein each of R₁ and R₉ is independently
selected from hydrido, lower alkyl, alkoxyacyl,
alkoxycarbonyl, benzyloxycarbonyl, haloalkyl and benzyl,
30 and wherein the nitrogen atom to which R₁ and R₉ are
attached may be combined with oxygen to form an N-oxide;
wherein R₂ is selected from hydrido, methyl, ethyl and
isopropyl; wherein R₃ is selected from benzyl, phenethyl,

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cyclohexylmethyl, pyrrolidinyl, piperidinyl,
pyrrolidinylmethyl, piperidinylmethyl, pyrazolemethyl,
pyrazoleethyl, pyridylmethyl, pyridylethyl,
thiazolemethyl, thiazoleethyl, imidazolemethyl,
5 imidazoleethyl, thienylmethyl, thienylethyl,
furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl,
isoxazolemethyl, isoxazoleethyl, pyridazinemethyl,
pyridazineethyl, pyrazinemethyl and pyrazineethyl;

10 wherein each of R4 and R6 is independently selected from
hydrido and methyl; wherein each of R5 and R8 is
independently selected from

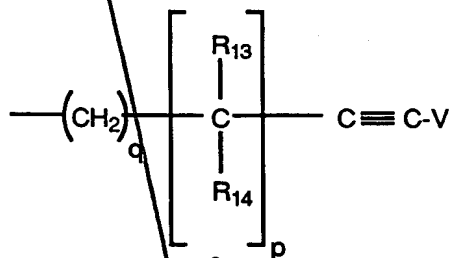


15 wherein V is selected from hydrido, alkyl and
trifluoromethyl; wherein each of R13 and R14 is a
radical independently selected from hydrido, alkyl and
alkynyl; wherein R7 is cyclohexylmethyl; wherein each of
20 R11 and R12 is independently selected from hydrido,
alkyl, dialkylamino and phenyl; wherein m is zero;
wherein n is a number selected from zero through five;
wherein p is a number selected from zero through five;
and wherein q is a number selected from zero through
25 five; or a pharmaceutically-acceptable salt thereof.

5. Compound of Claim 4 wherein A is selected
from CO and SO2; wherein X is selected from oxygen atom
and methylene; wherein each of R1 and R9 is independently
30 selected from hydrido, methyl, ethyl, n-propyl, isopropyl,
benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and
methoxymethylcarbonyl, and wherein the nitrogen atom to
which R1 and R9 are attached may be combined with oxygen

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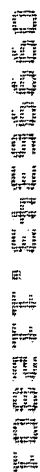
to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, cyclohexylmethyl, phenethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, methyl, ethyl, propyl and ethynyl; wherein R₇ is cyclohexylmethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

6. Compound of Claim 5 wherein A is selected from CO and SO₂; wherein X is selected from oxygen atom and methylene; wherein each of R₁ and R₉ is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein

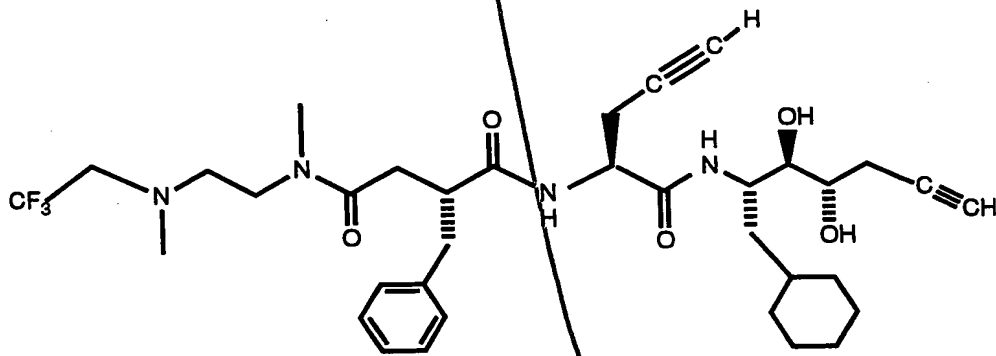
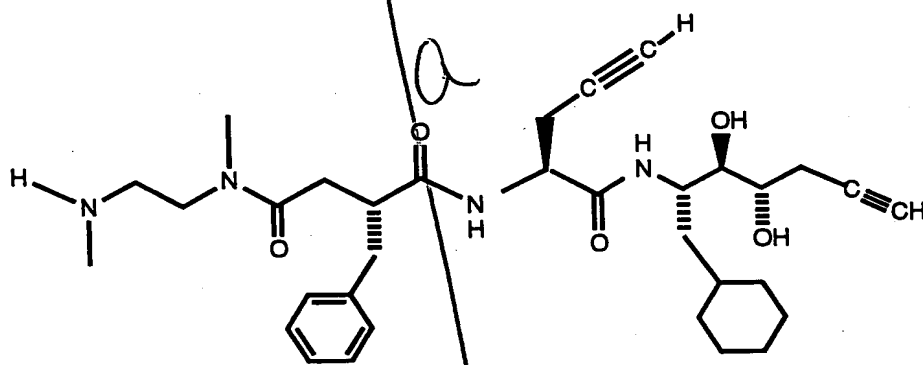
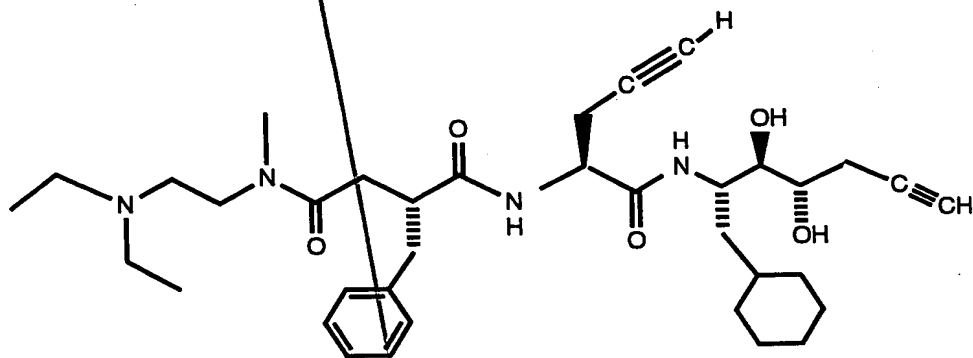
Abstract—The purpose of this study was to determine the effect of a 10-week training program on the heart rate (HR) and heart rate reserve (HRR) of sedentary, middle-aged men. The subjects were 15 men, 40 to 50 years of age, who were sedentary and had no cardiovascular disease. They were randomly assigned to a 10-week training program or a control group. The training program consisted of 30 minutes of aerobic exercise, 3 times per week, at 70% of the maximum HR. The control group did not exercise. The HR and HRR were measured at rest and during maximal exercise at the beginning and at the end of the 10-week period. The HR and HRR were significantly higher at the end of the 10-week period in the training group compared to the control group. The results of this study suggest that a 10-week training program can improve the HR and HRR of sedentary, middle-aged men.



Abstract—The purpose of this study was to determine the effect of a 10-week training program on the heart rate (HR) and heart rate reserve (HRR) of sedentary, middle-aged men. The subjects were 15 men, 40 to 50 years of age, who were sedentary and had no cardiovascular disease. They were randomly assigned to a 10-week training program or a control group. The training program consisted of 30 minutes of aerobic exercise, 3 times per week, at 70% of the maximum HR. The control group did not exercise. The HR and HRR were measured at rest and during maximal exercise at the beginning and at the end of the 10-week period. The HR and HRR were significantly higher at the end of the 10-week period in the training group compared to the control group. The results of this study suggest that a 10-week training program can improve the HR and HRR of sedentary, middle-aged men.

7. Compound of Claim 6 selected from compounds, their tautomers, and the pharmaceutically-acceptable esters and salts thereof, of the group consisting of

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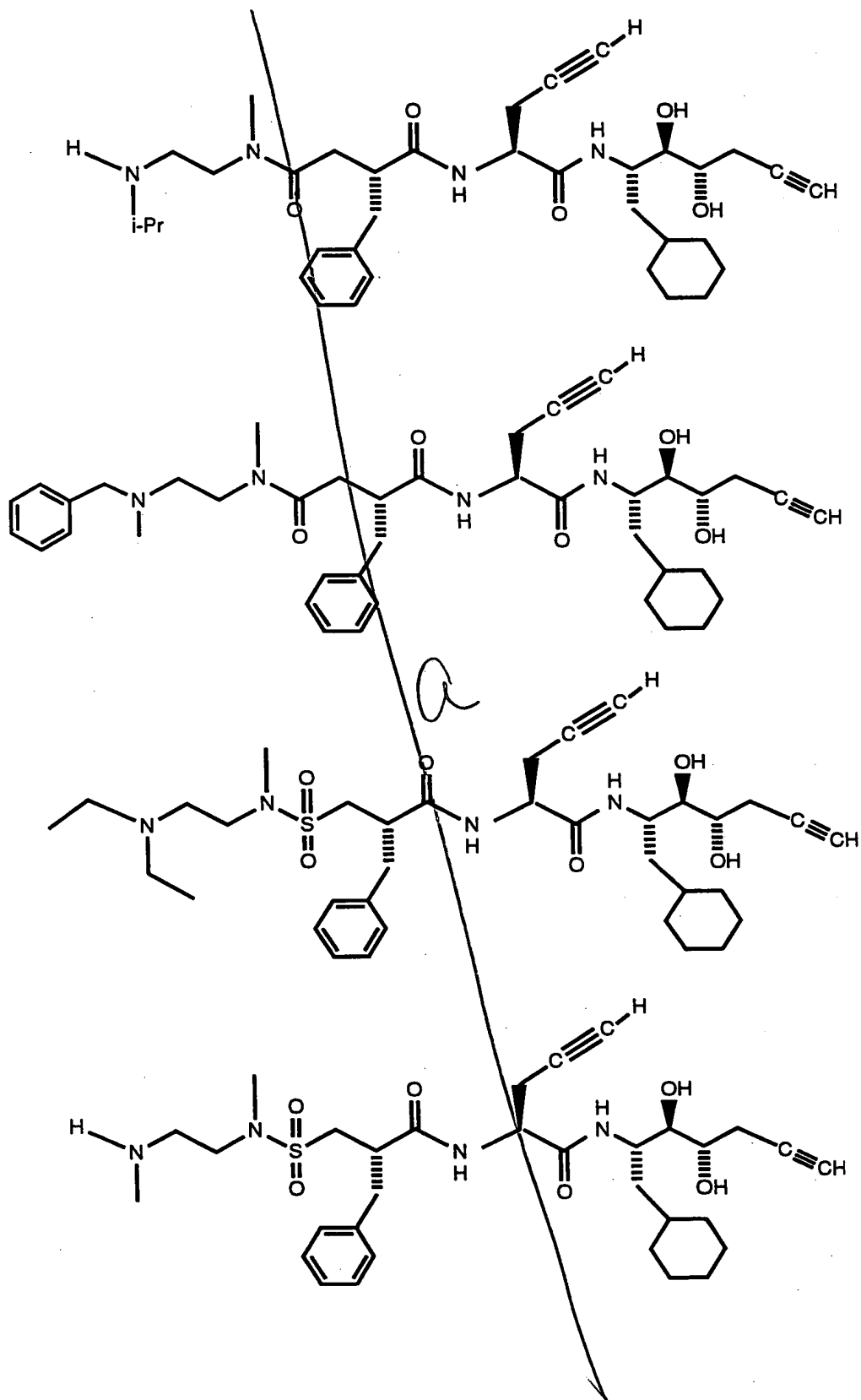


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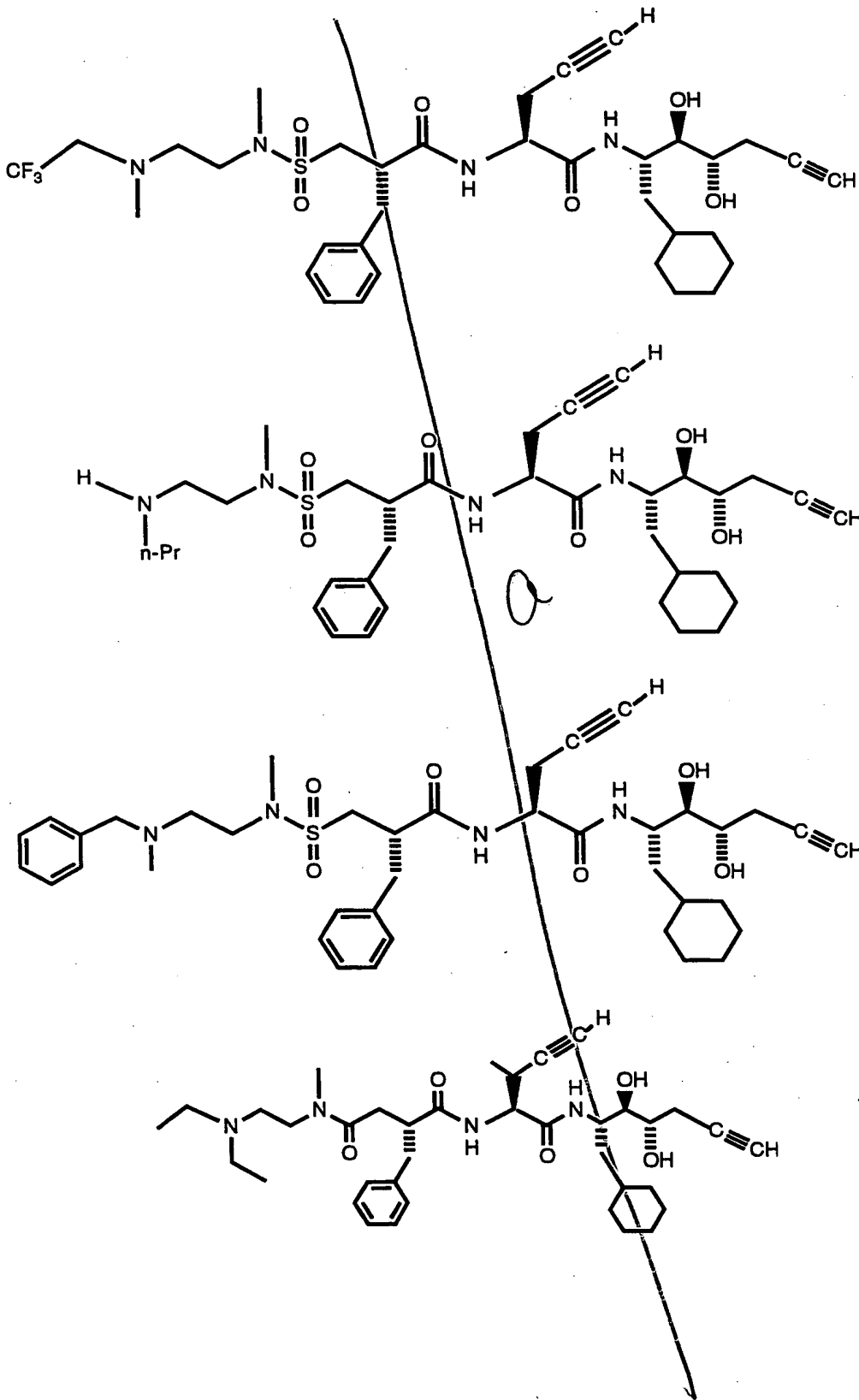
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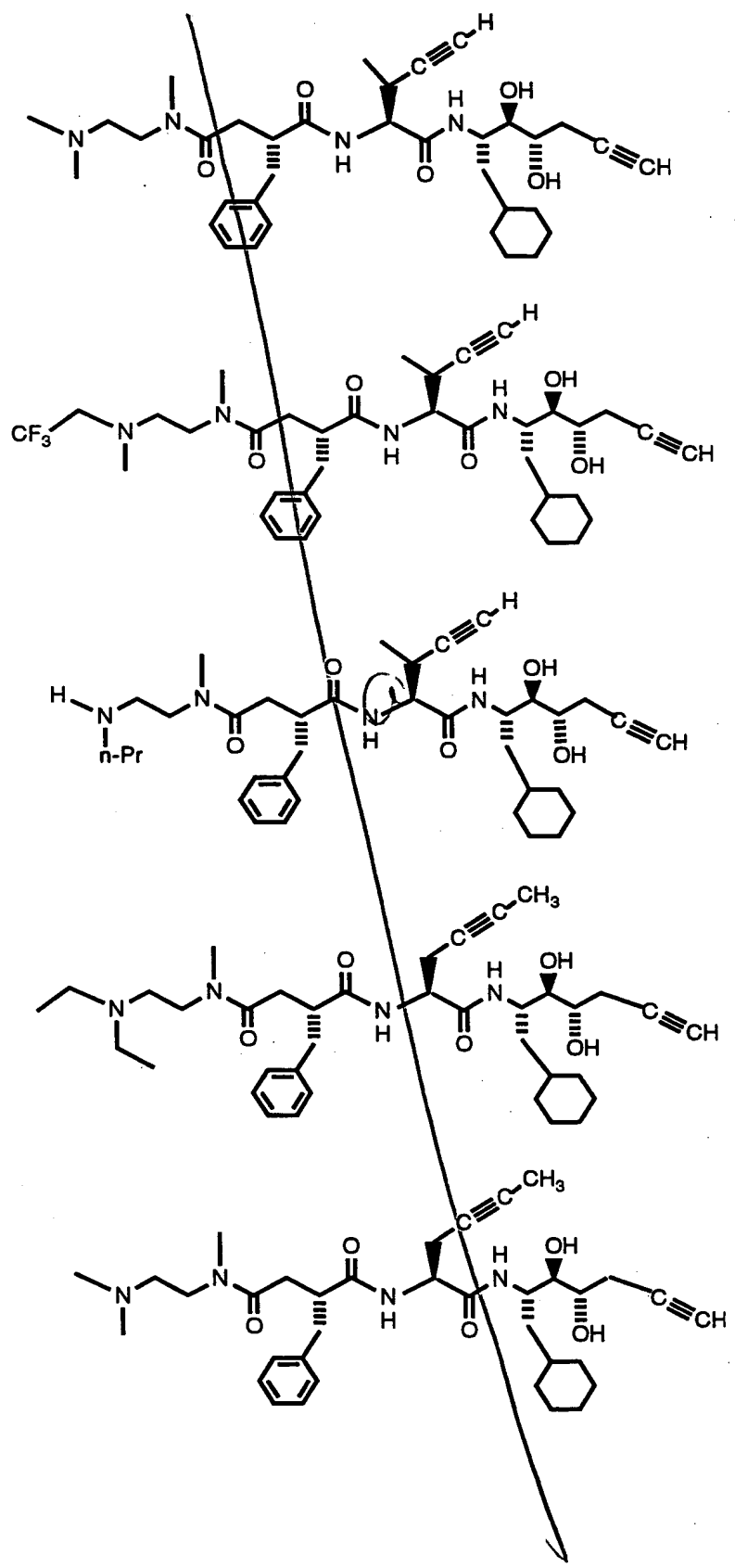
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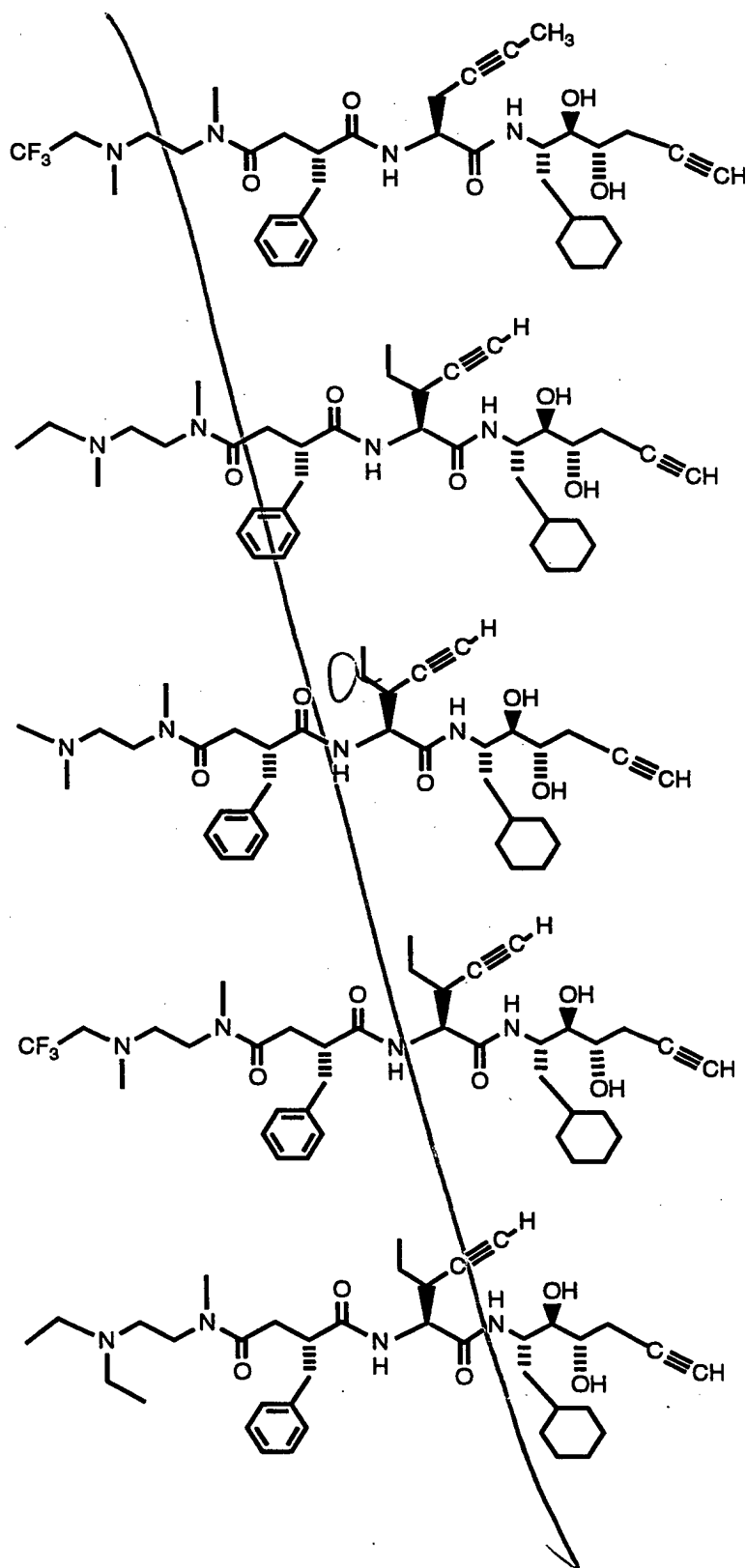
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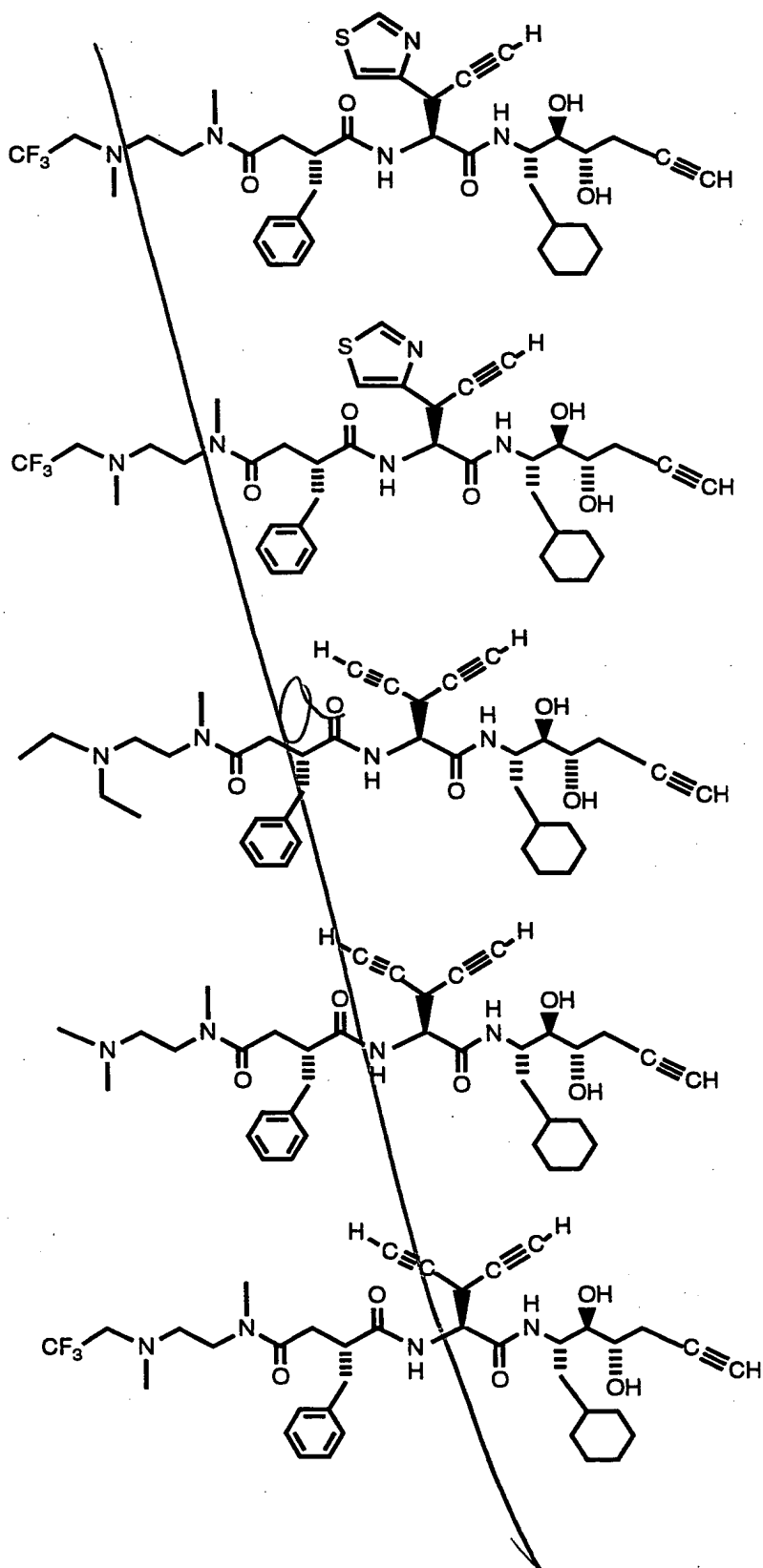


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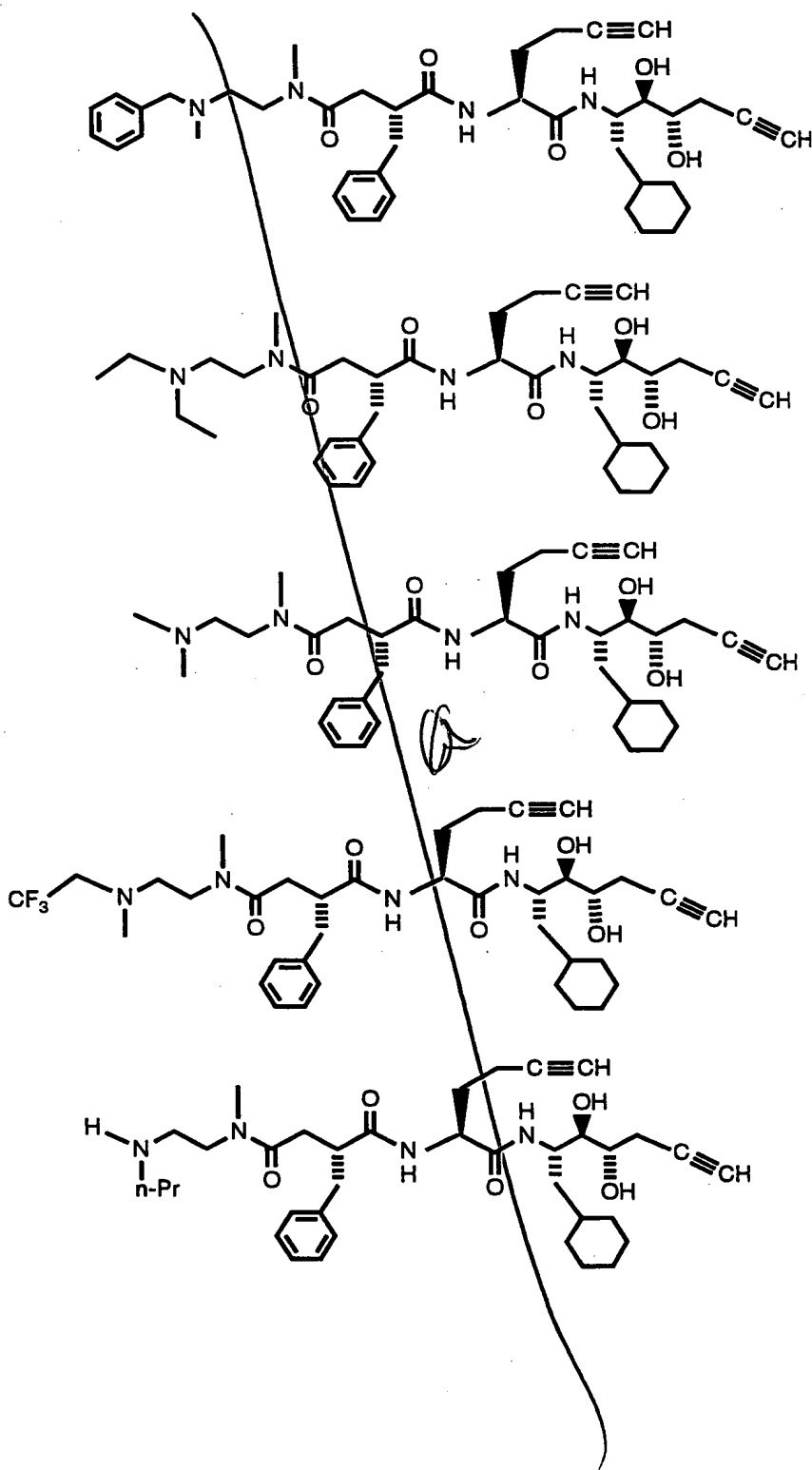
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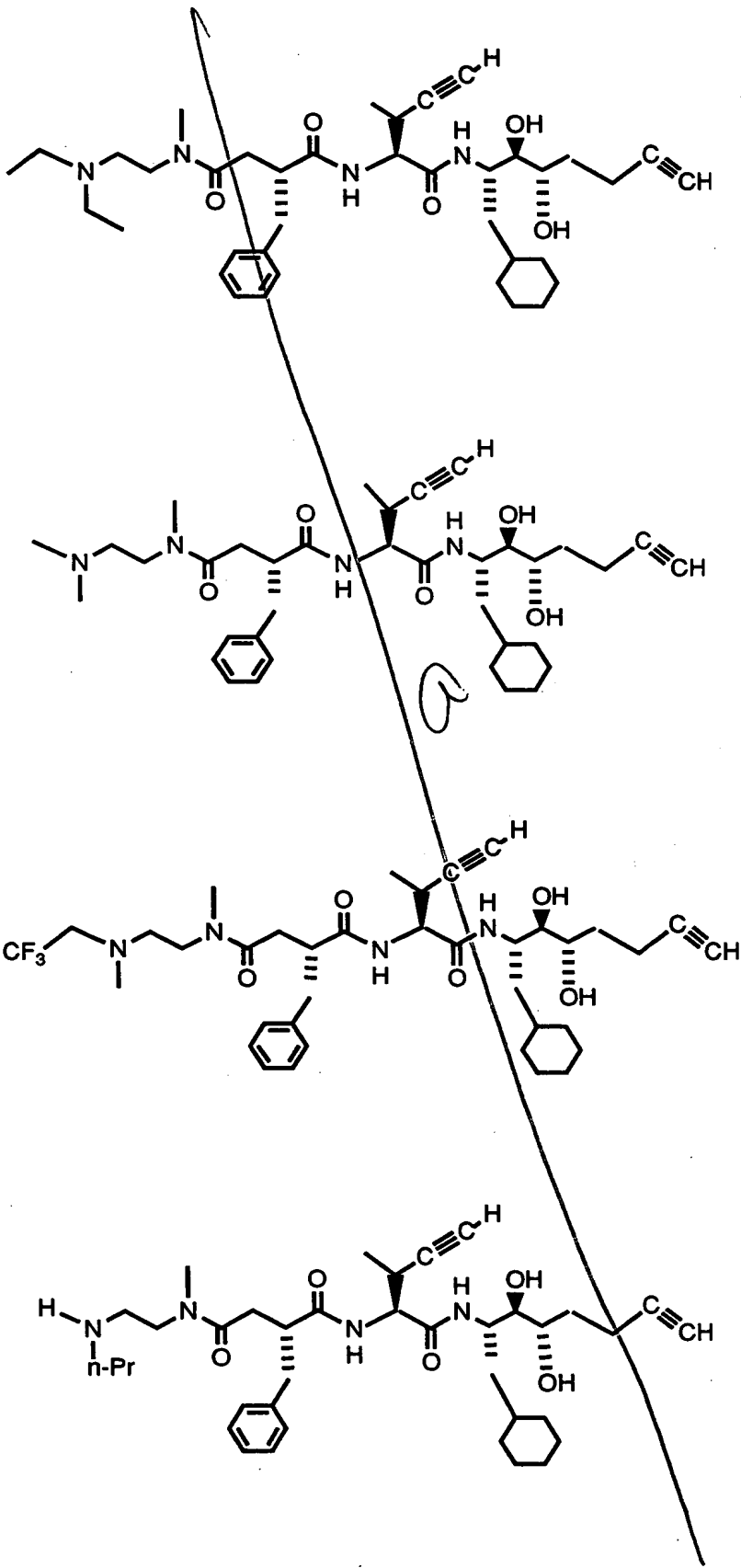
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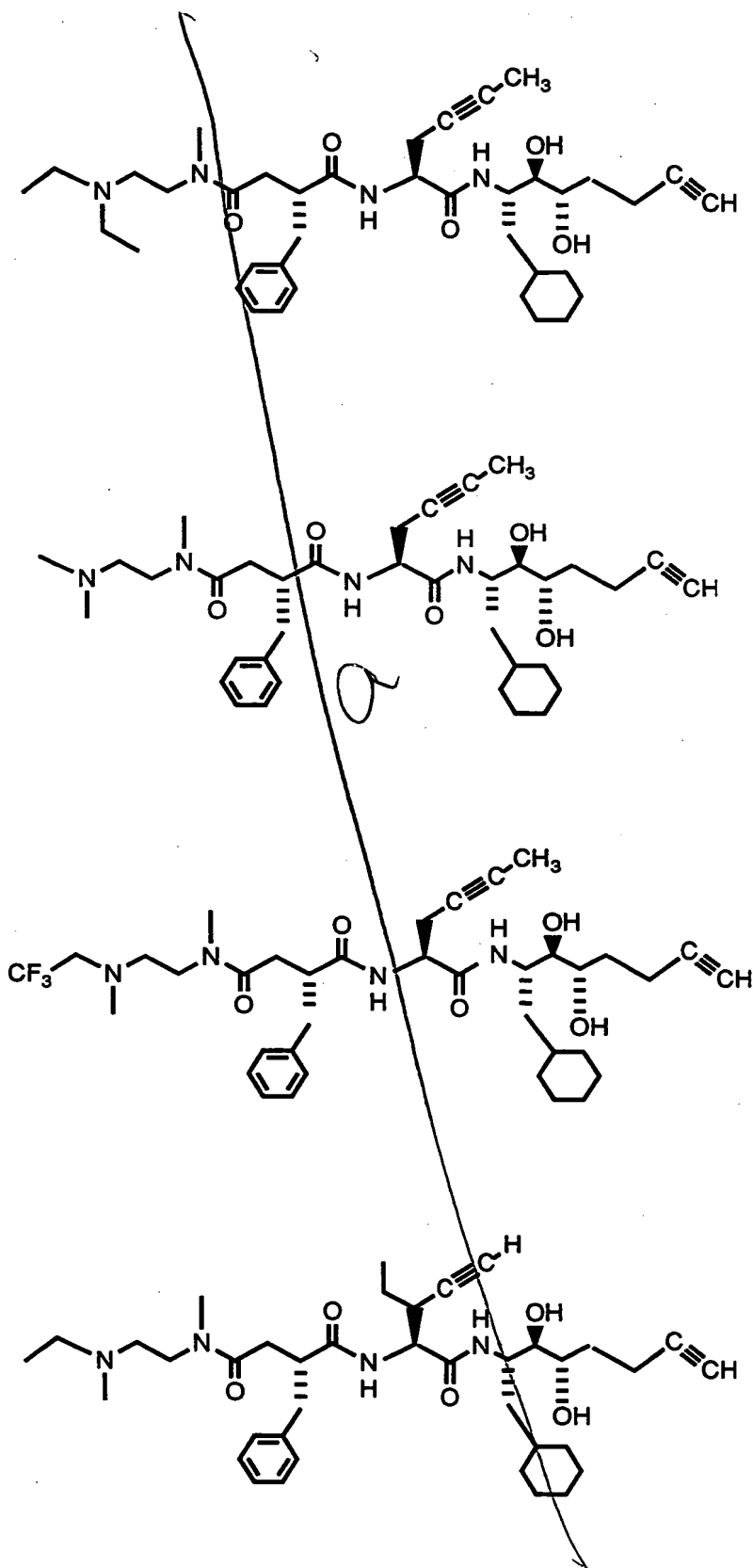
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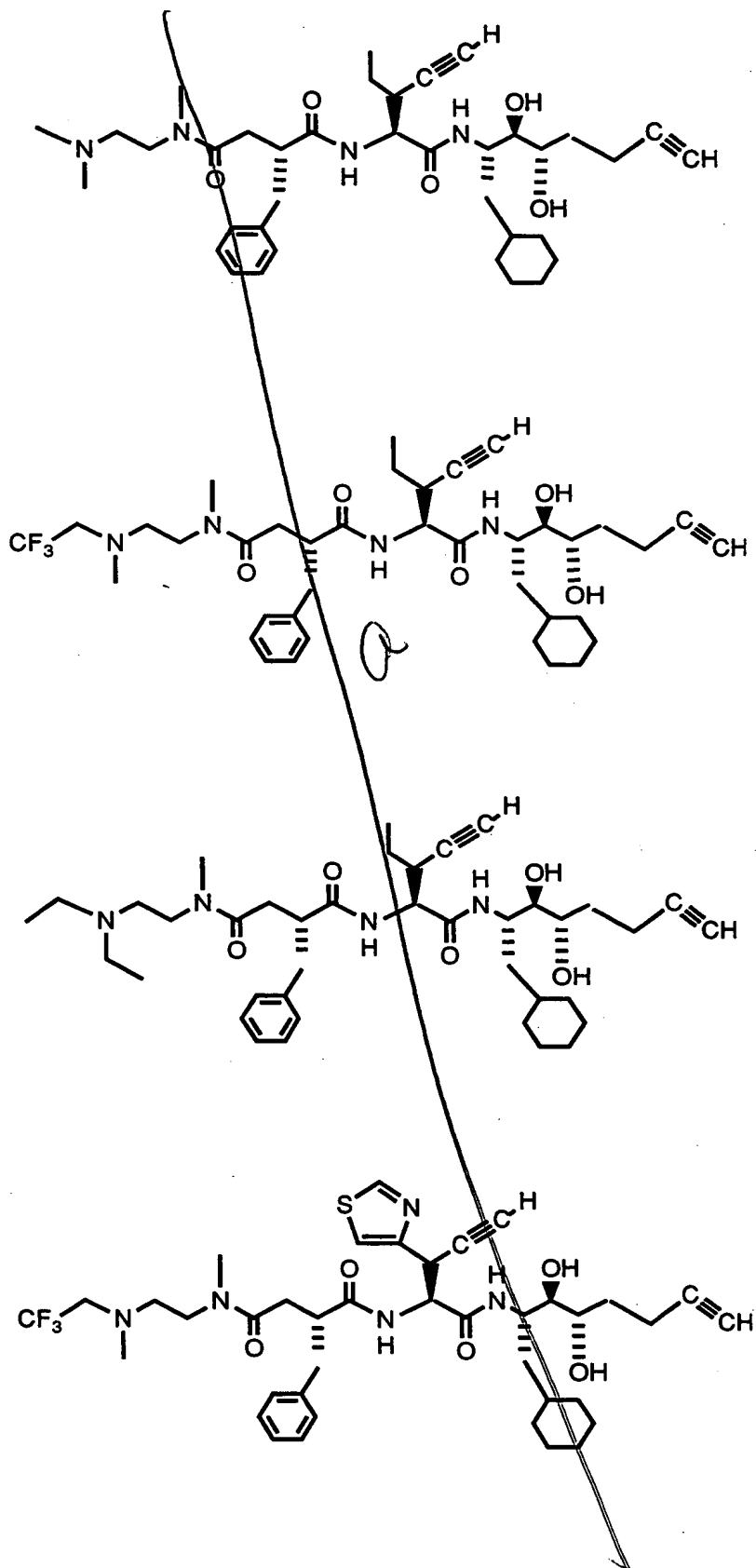
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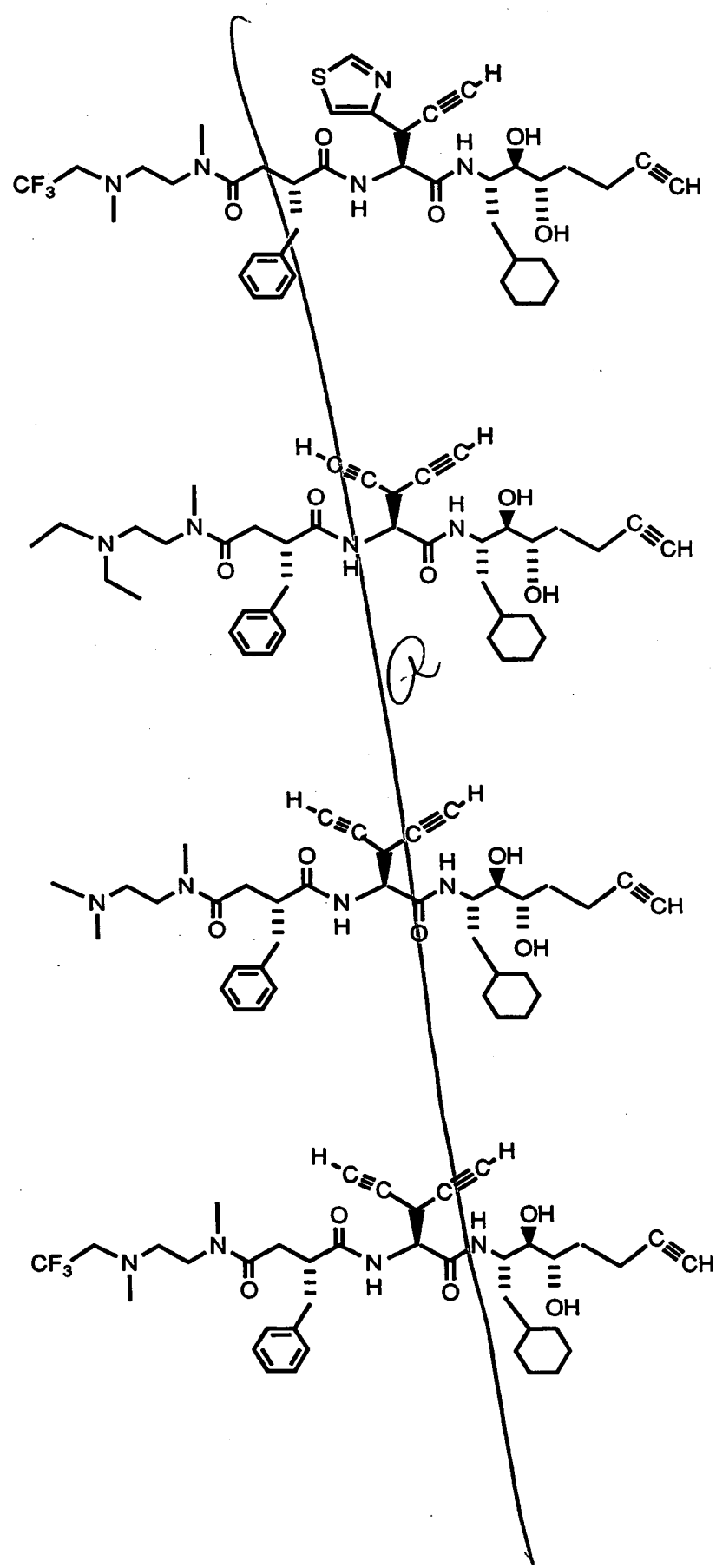
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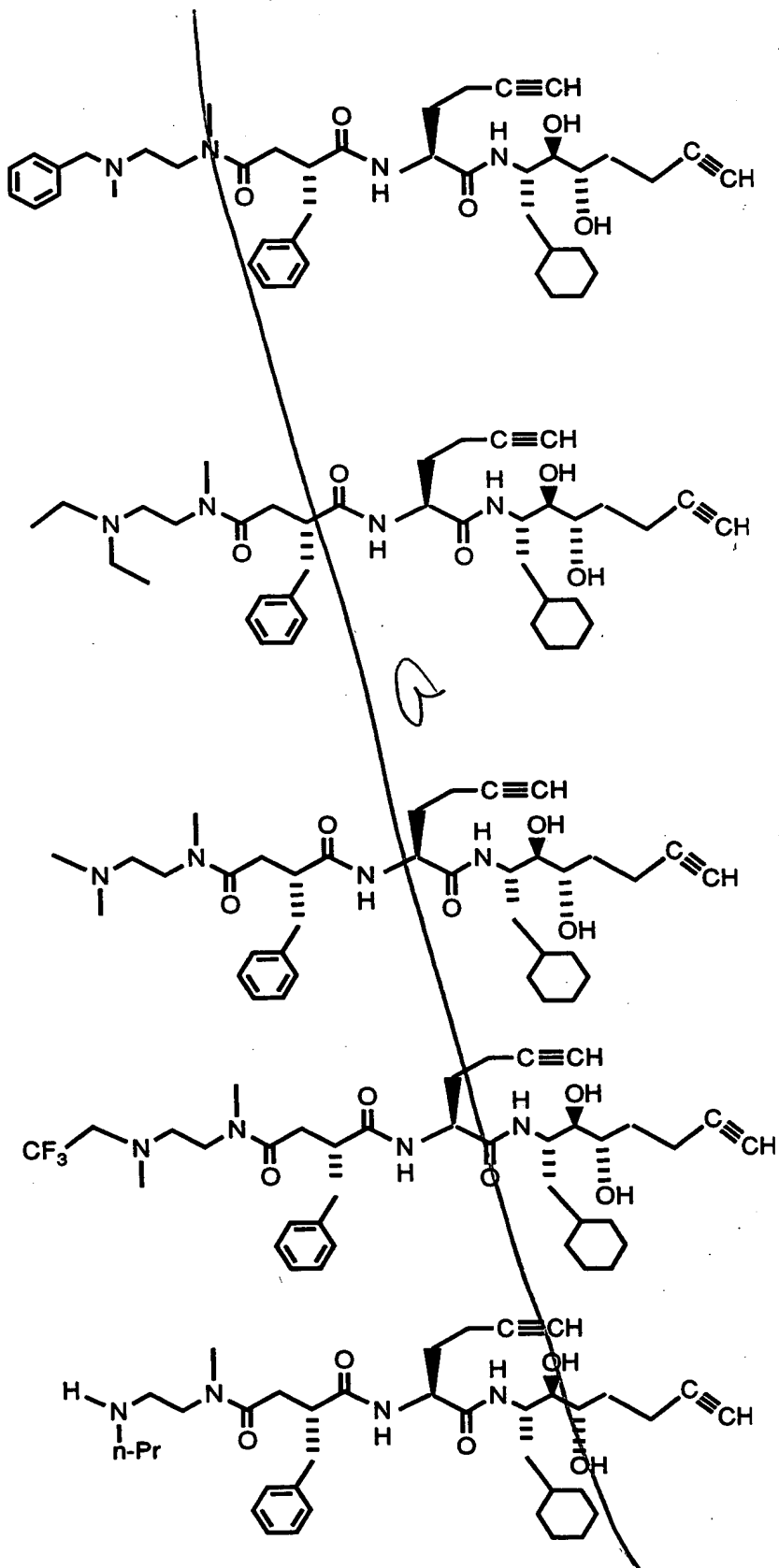


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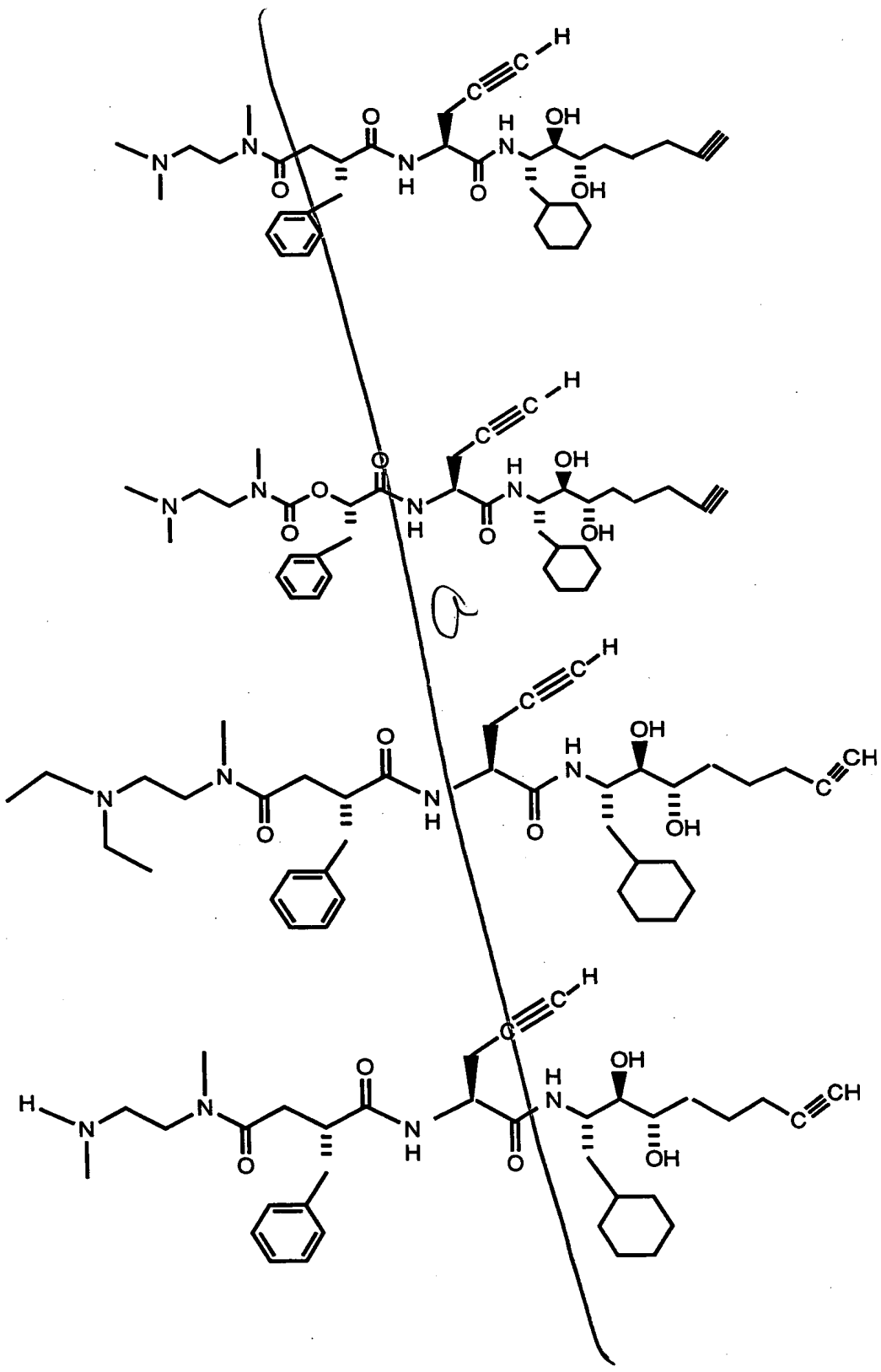
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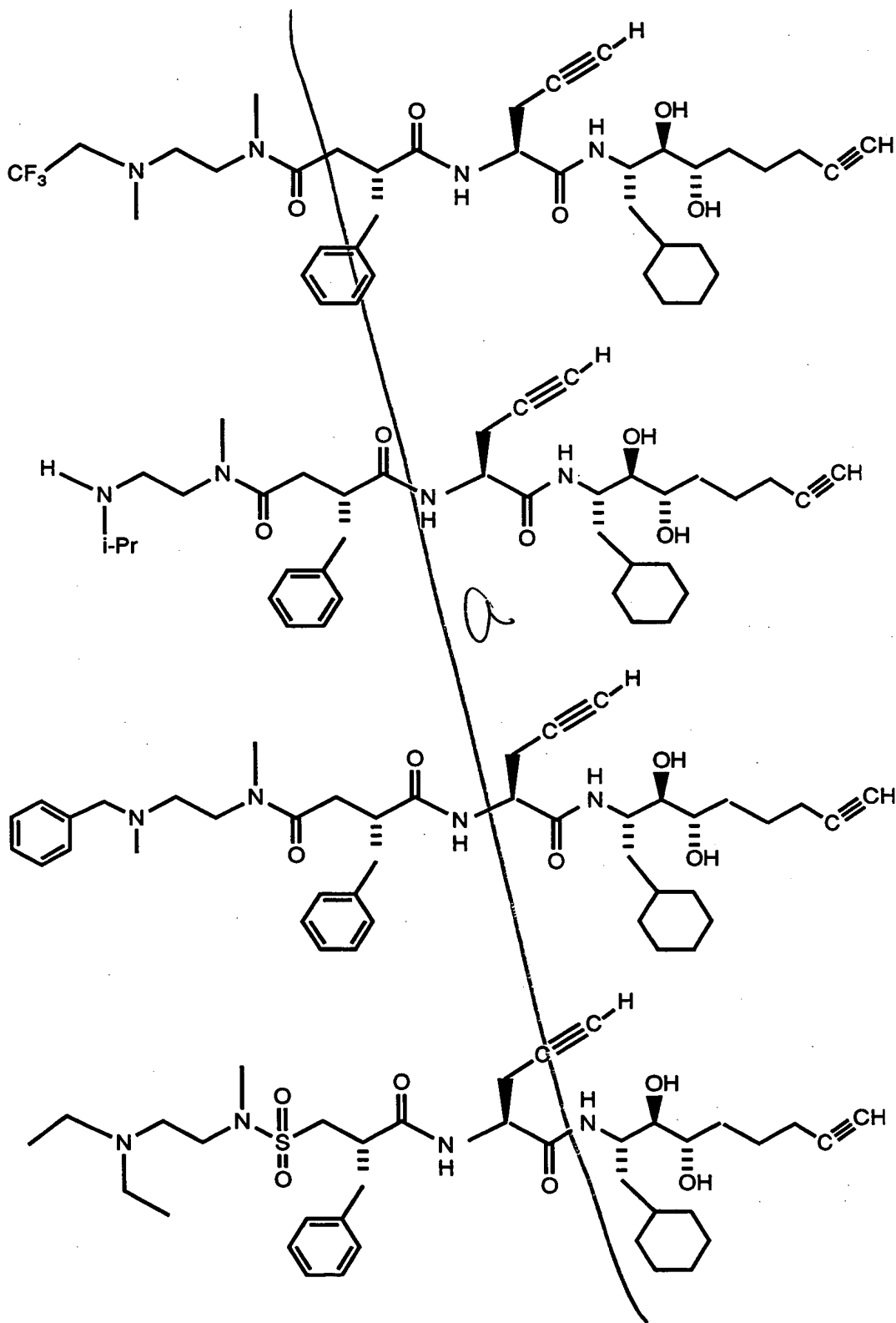
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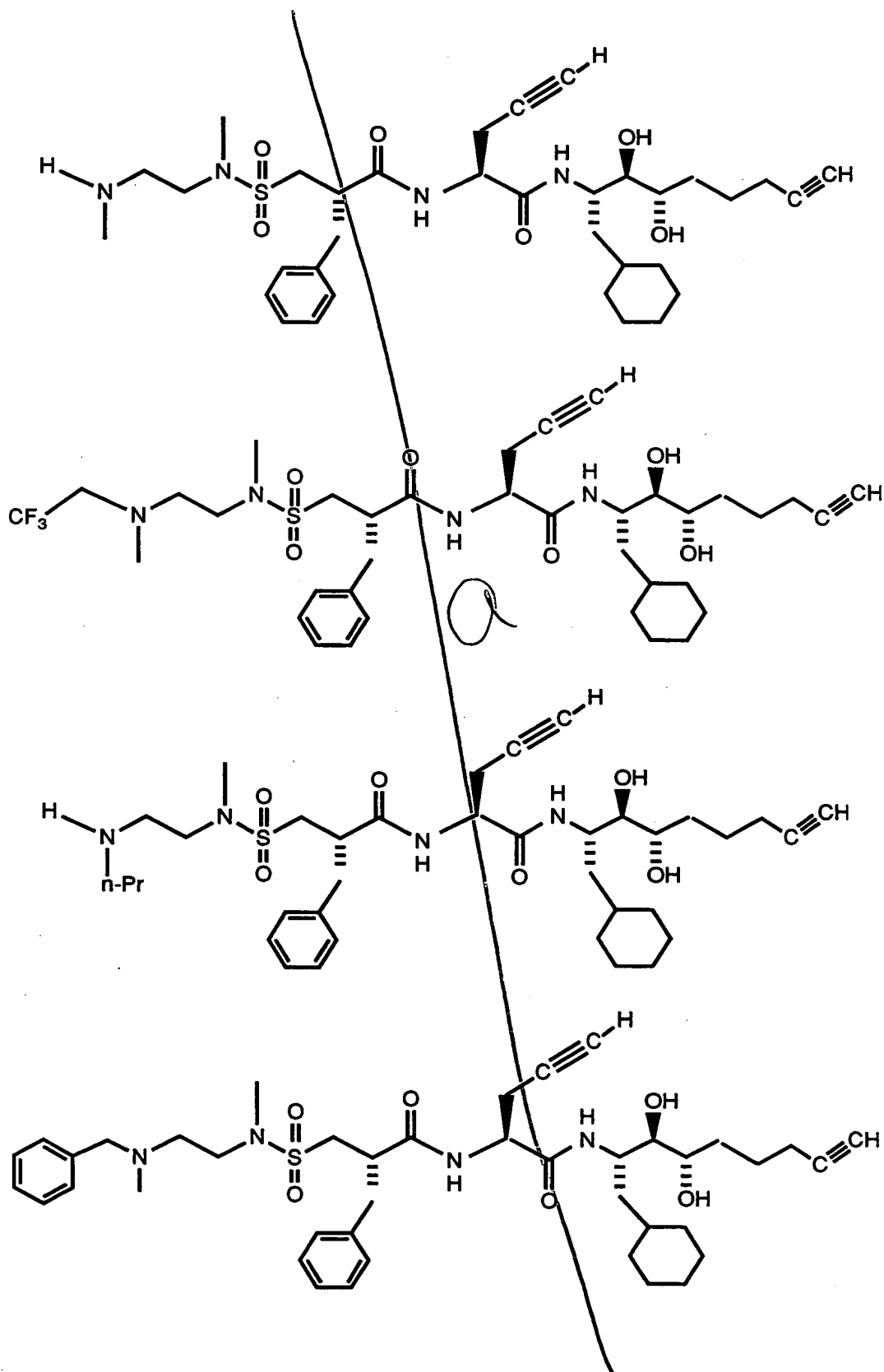
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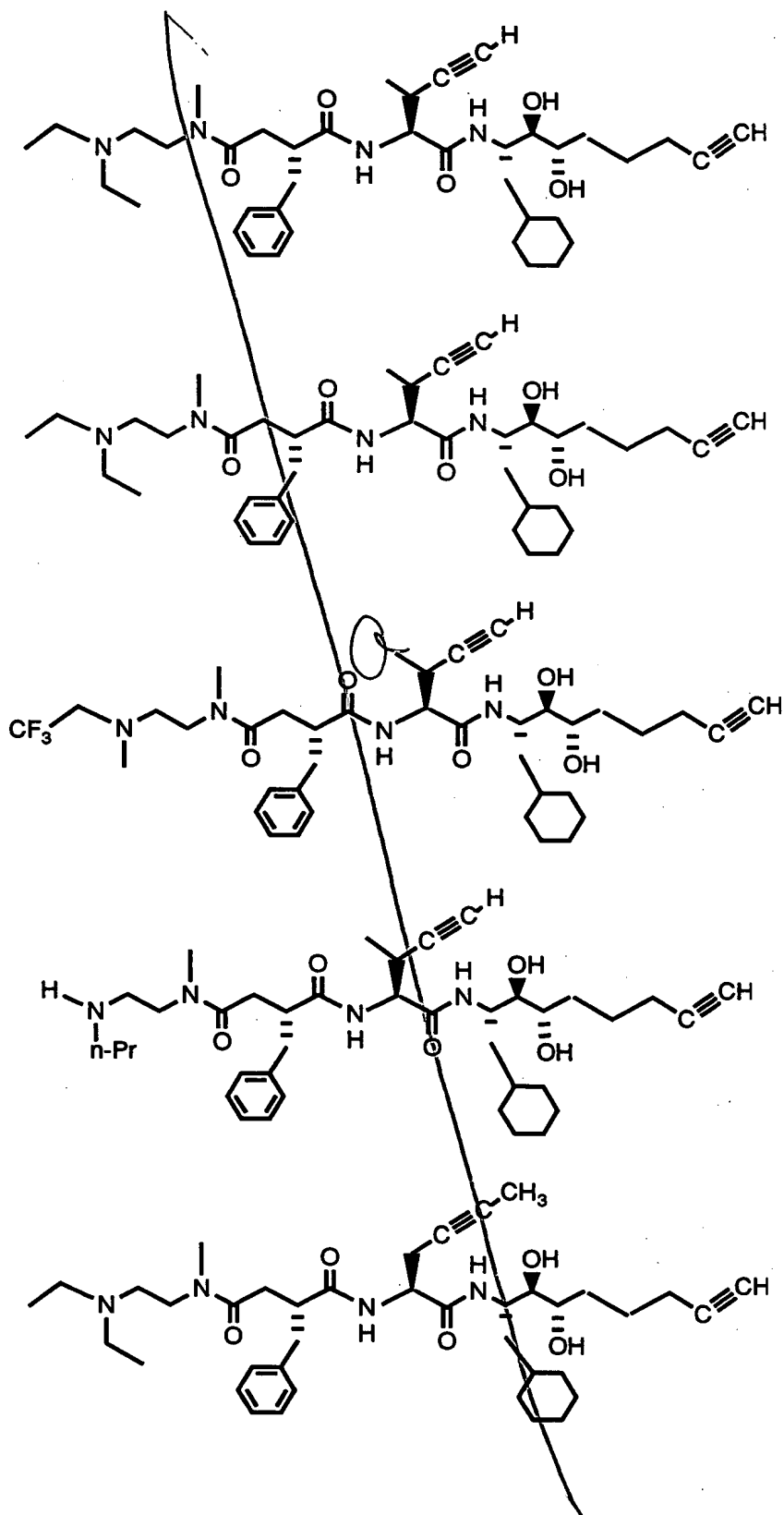
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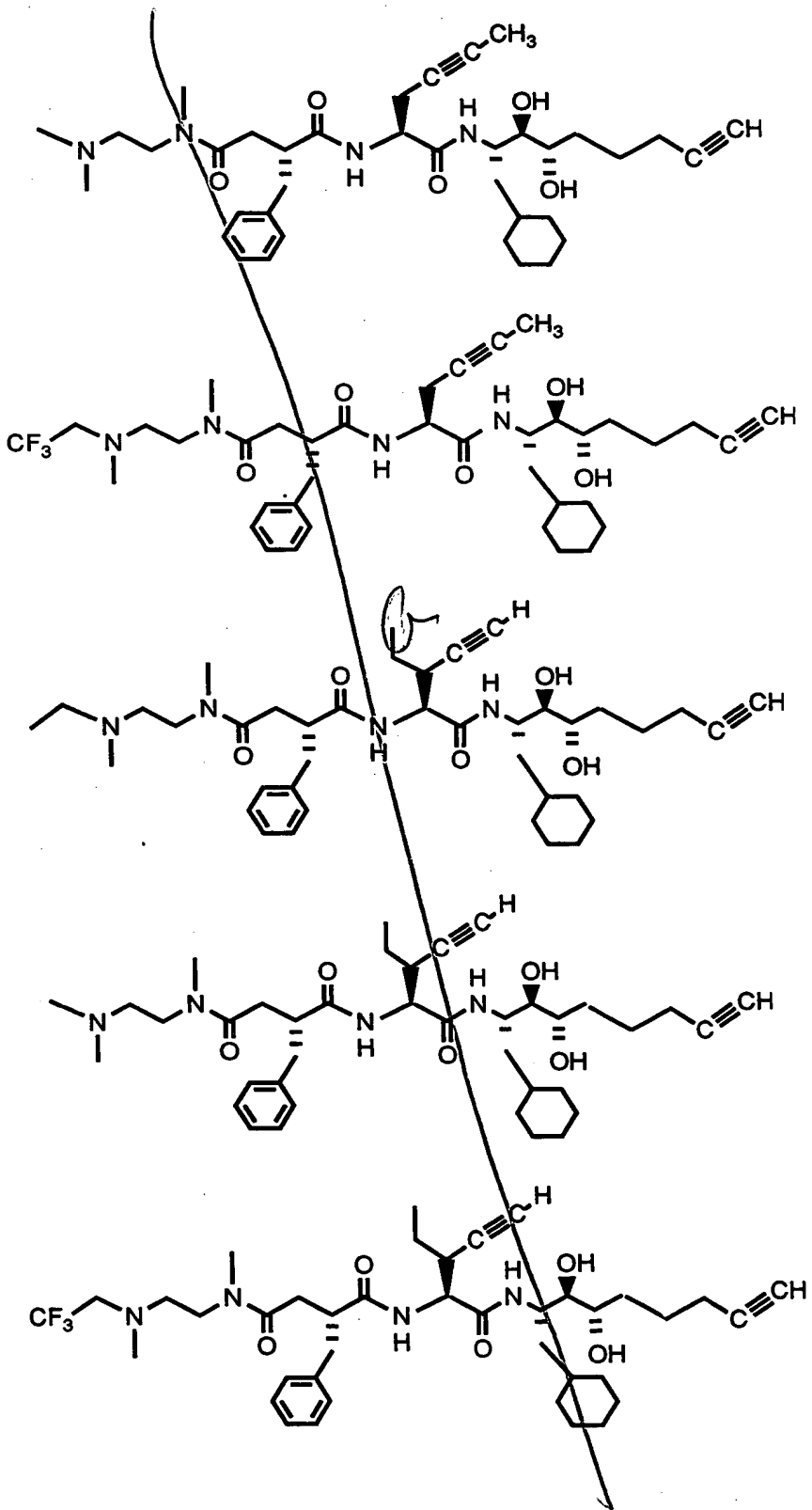
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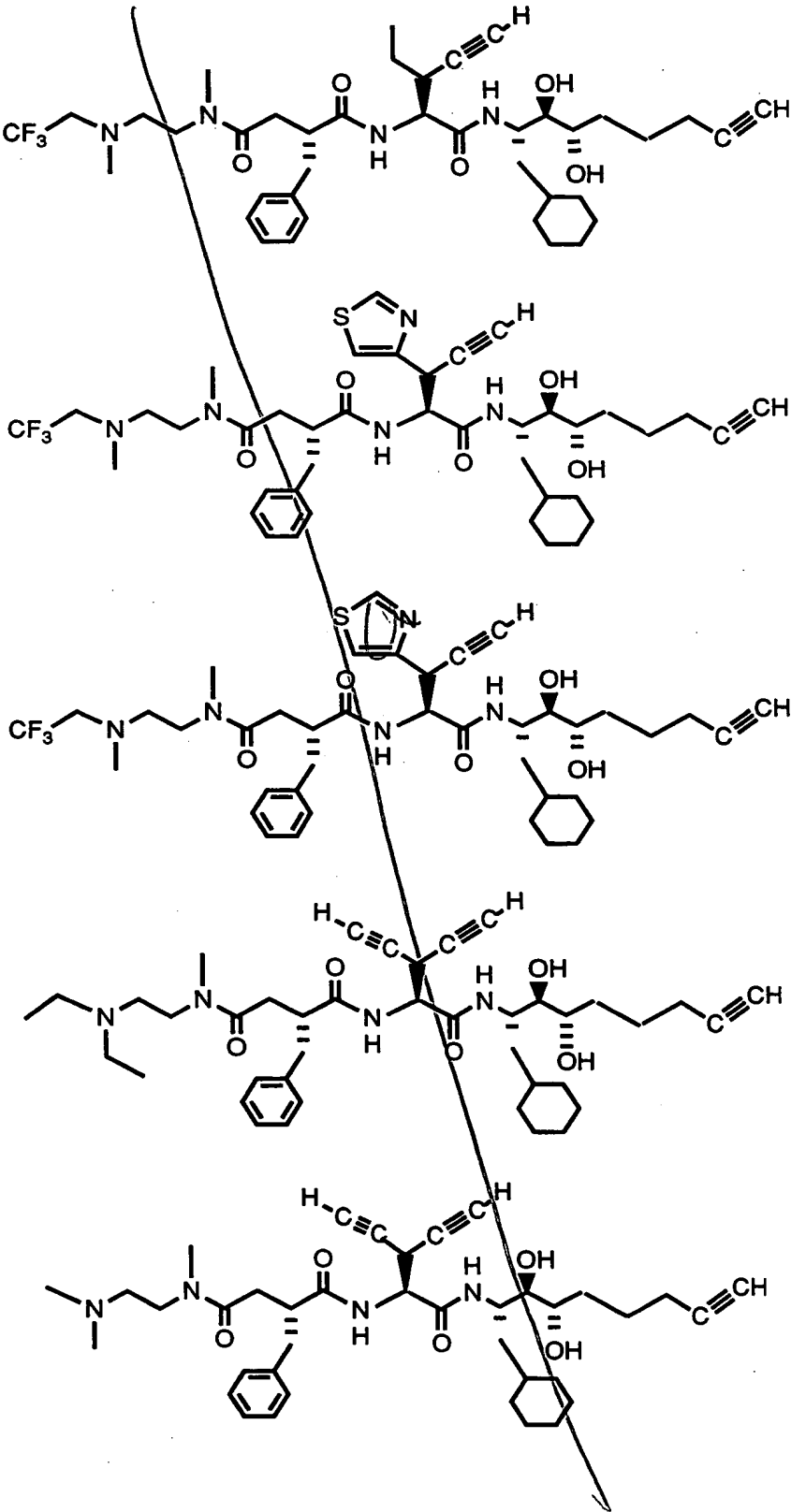


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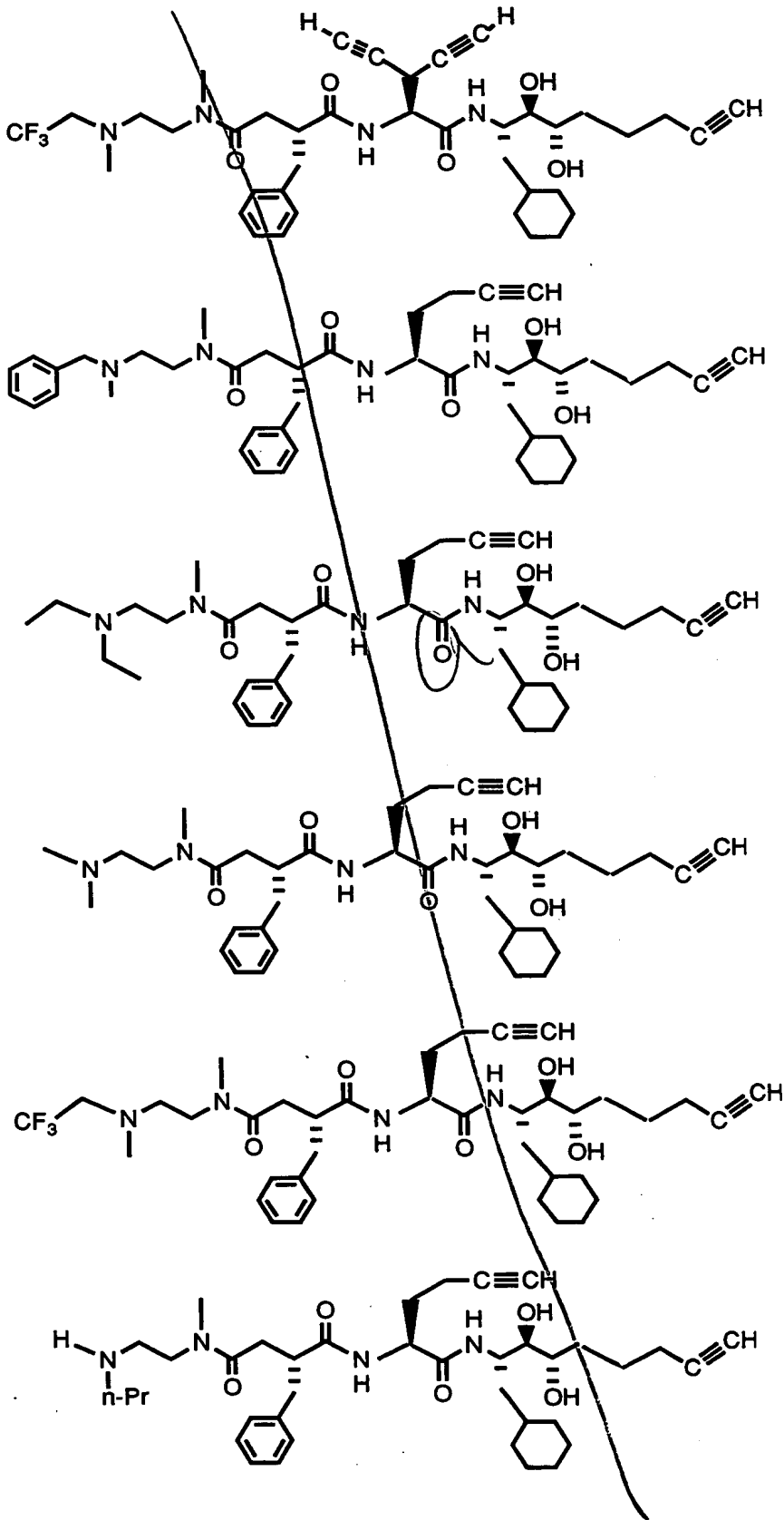
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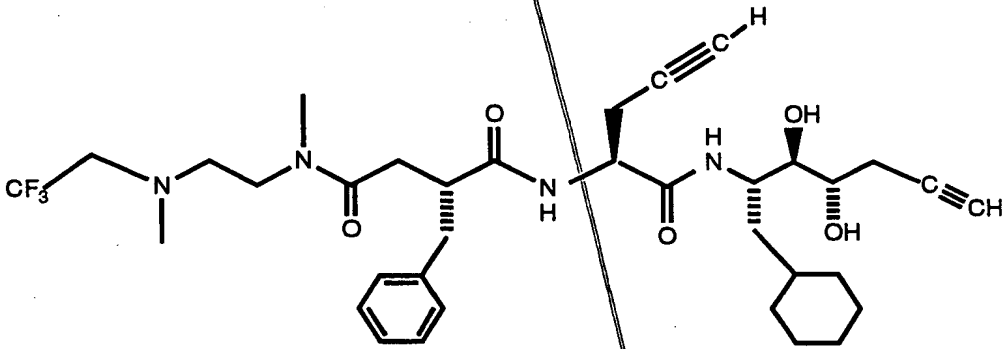
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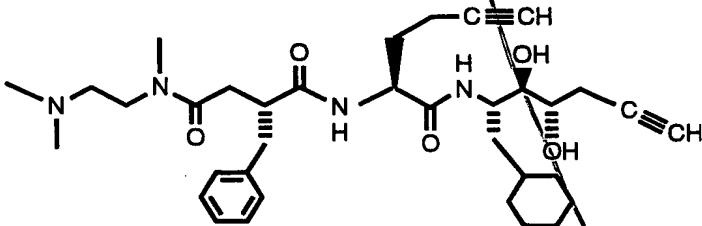
8. Compound of Claim 6 which is N1-[1R*-
[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-
hexynyl]amino]carbonyl]-3-butynyl]-N4-[2-
5 (dimethylamino)ethyl]-N4-methyl-2S*-(
(phenylmethyl)butanediamide or a pharmaceutically-
acceptable salt thereof.

9. Compound of Claim 6 which is [1R*-
10 [[1R*-[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-
hexynyl]amino]carbonyl]-3-butynyl]amino]carbonyl]-2-
phenylethyl)[2-(dimethylamino)ethyl]methylcarbamate or a
pharmaceutically-acceptable salt thereof.

15 10. Compound of Claim 6 which is

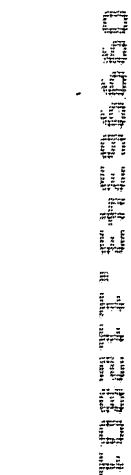


20 11. Compound of Claim 6 which is



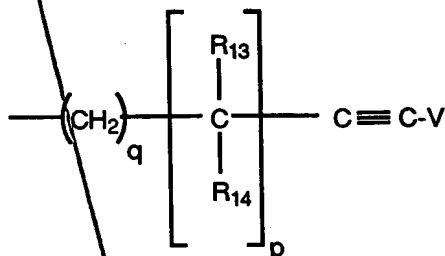
or a pharmaceutically-acceptable salt thereof.

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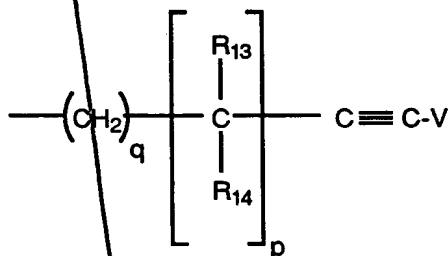
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and cycloalkyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl, cycloalkyl, haloalkyl, benzyl and phenyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, phenyl, heterocyclic, heterocyclical and heterocycliccycloalkyl; wherein R₇ is selected from substituted or unsubstituted alkyl, cycloalkyl, phenyl, cycloalkylalkyl and phenylalkyl, any one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo, haloalkyl, alkenyl, alkynyl and cyano; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, haloalkyl, dialkylamino and phenyl; and wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

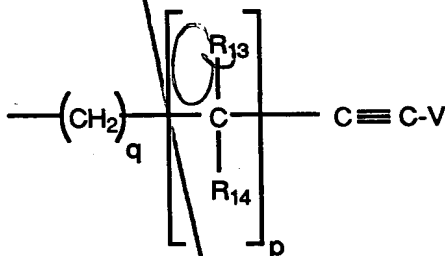
13. The composition of Claim 12 wherein A is selected from methylene, CO, SO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido, alkyl and benzyl; wherein each of R₁ and R₉ is independently selected from hydrido, lower alkyl, haloalkyl, cycloalkyl, alkoxycarbonyl, benzyloxycarbonyl, loweralkanoyl, alkoxyacyl, phenyl and benzyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an



wherein V is selected from hydrido, alkyl, haloalkyl, benzyl and phenyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, heteroarylalkyl and heteroarylcycloalkyl; wherein R₇ is selected from substituted or unsubstituted cyclohexylmethyl and benzyl, either one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo and haloalkyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

14. The composition of Claim 13 wherein A is selected from methylene, CO, SO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido, alkyl and benzyl; wherein each of R₁ and R₉ is independently selected from hydrido, alkyl, alkoxyacyl, haloalkyl, alkoxycarbonyl, benzyloxycarbonyl, and benzyl, and wherein the nitrogen

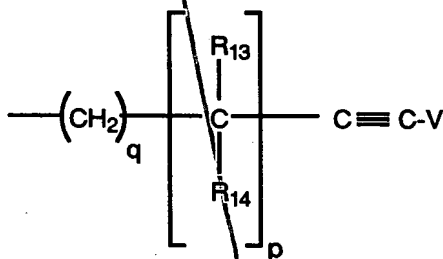
atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein each of R₂, R₄ and R₆ is independently selected from hydrido and alkyl; wherein R₃ is selected from benzyl, phenethyl, cyclohexylmethyl, phenpropyl, pyrrolidinyl, piperidinyl, pyrrolidinylmethyl, piperidinylmethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl and haloalkyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, thiazole and thiazolemethyl; wherein R₇ is cyclohexylmethyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

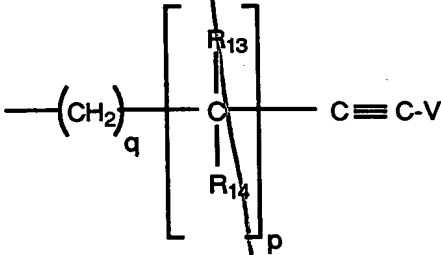
15. The composition of Claim 14 wherein A is selected from CO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from

hydrido and methyl; wherein each of R₁ and R₉ is independently selected from hydrido, lower alkyl, alkoxyacyl, alkoxy carbonyl, benzyloxycarbonyl, haloalkyl and benzyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, phenethyl, cyclohexylmethyl, pyrrolidinyl, piperidinyl, pyrrolidinylmethyl, piperidinylmethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl and alkynyl; wherein R₇ is cyclohexylmethyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

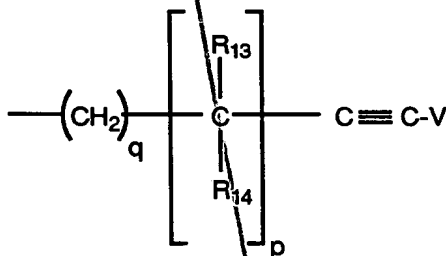
16. The composition of Claim 15 wherein A is selected from CO and SO₂; wherein X is selected from oxygen atom and methylene; wherein each of R₁ and R₉ is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, cyclohexylmethyl, phenethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, methyl, ethyl, propyl and ethynyl; wherein R₇ is cyclohexylmethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero; wherein n is a number selected from zero through five; wherein p is a number selected from zero through

five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

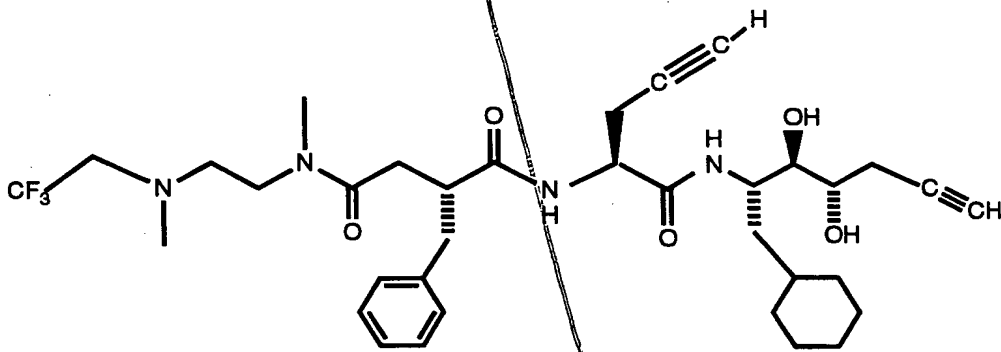
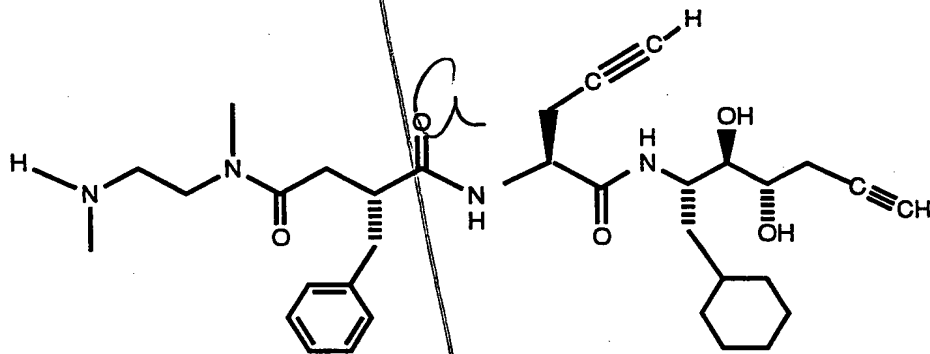
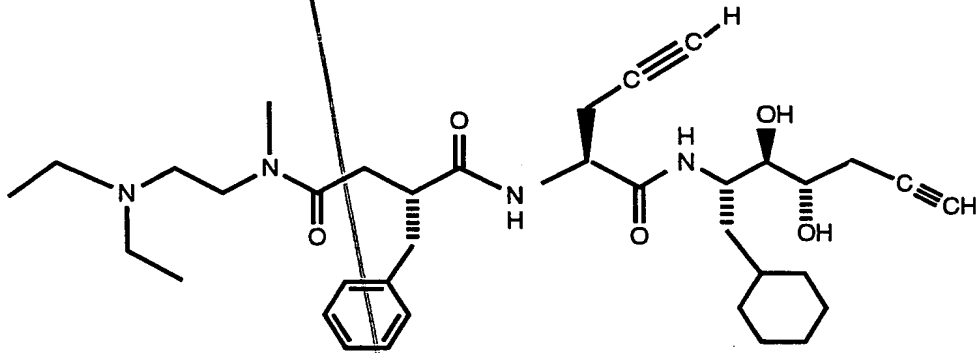
17. The composition of Claim 16 wherein A is selected from CO and SO₂; wherein X is selected from oxygen atom and methylene; wherein each of R₁ and R₉ is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, cyclohexylmethyl, phenethyl, imidazolemethyl, pyridylmethyl and 2-pyridylethyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, methyl and ethynyl; wherein R₇ is cyclohexylmethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl and phenyl; wherein m is zero; wherein n is a number selected from zero through three; wherein p is a number selected from one through three; and wherein q is zero or one; or a pharmaceutically-acceptable salt thereof.

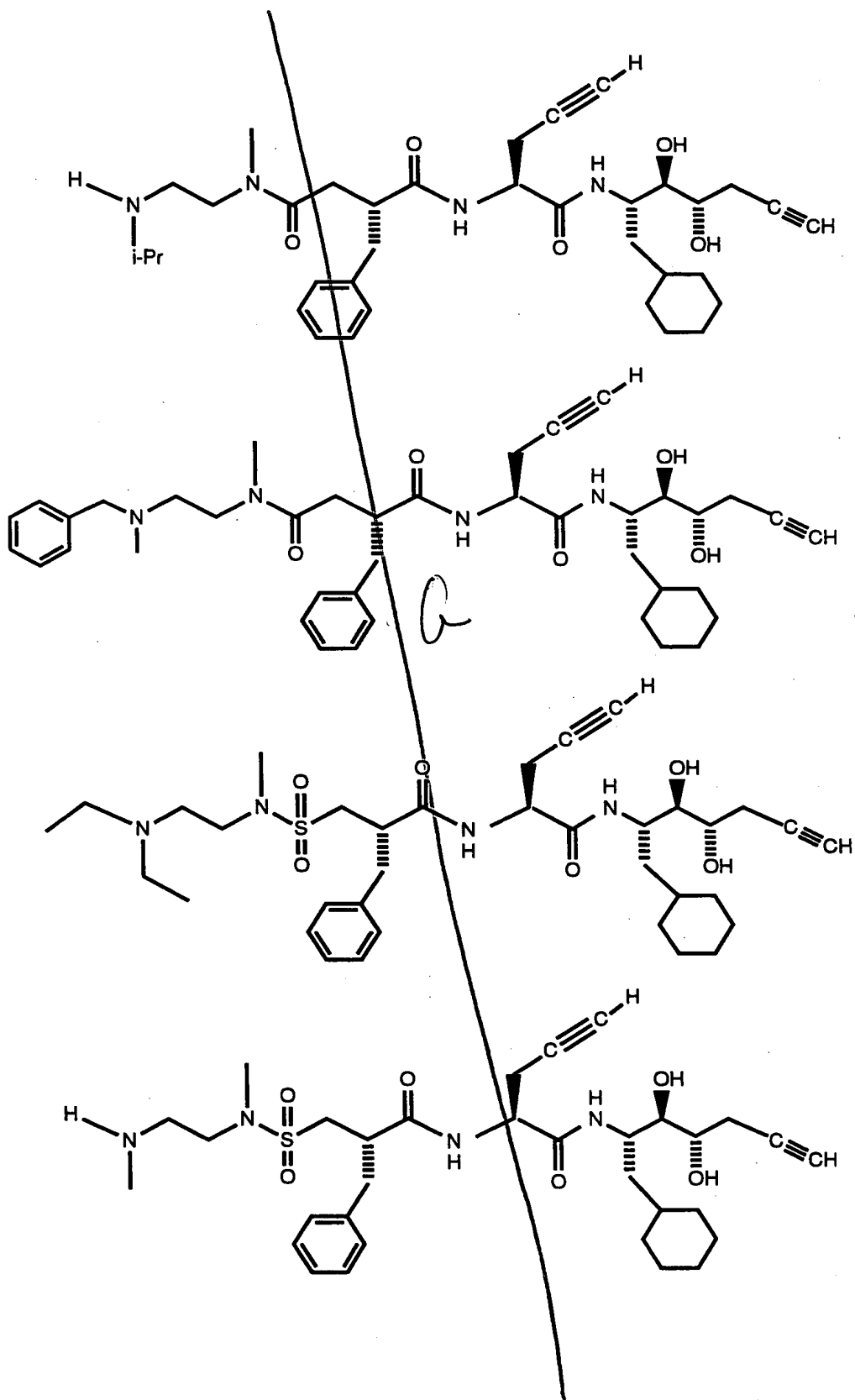
18. The composition of Claim 17 wherein said renin-inhibiting compound is selected from compounds, their tautomers, and the pharmaceutically-acceptable esters and salts thereof, of the group consisting of

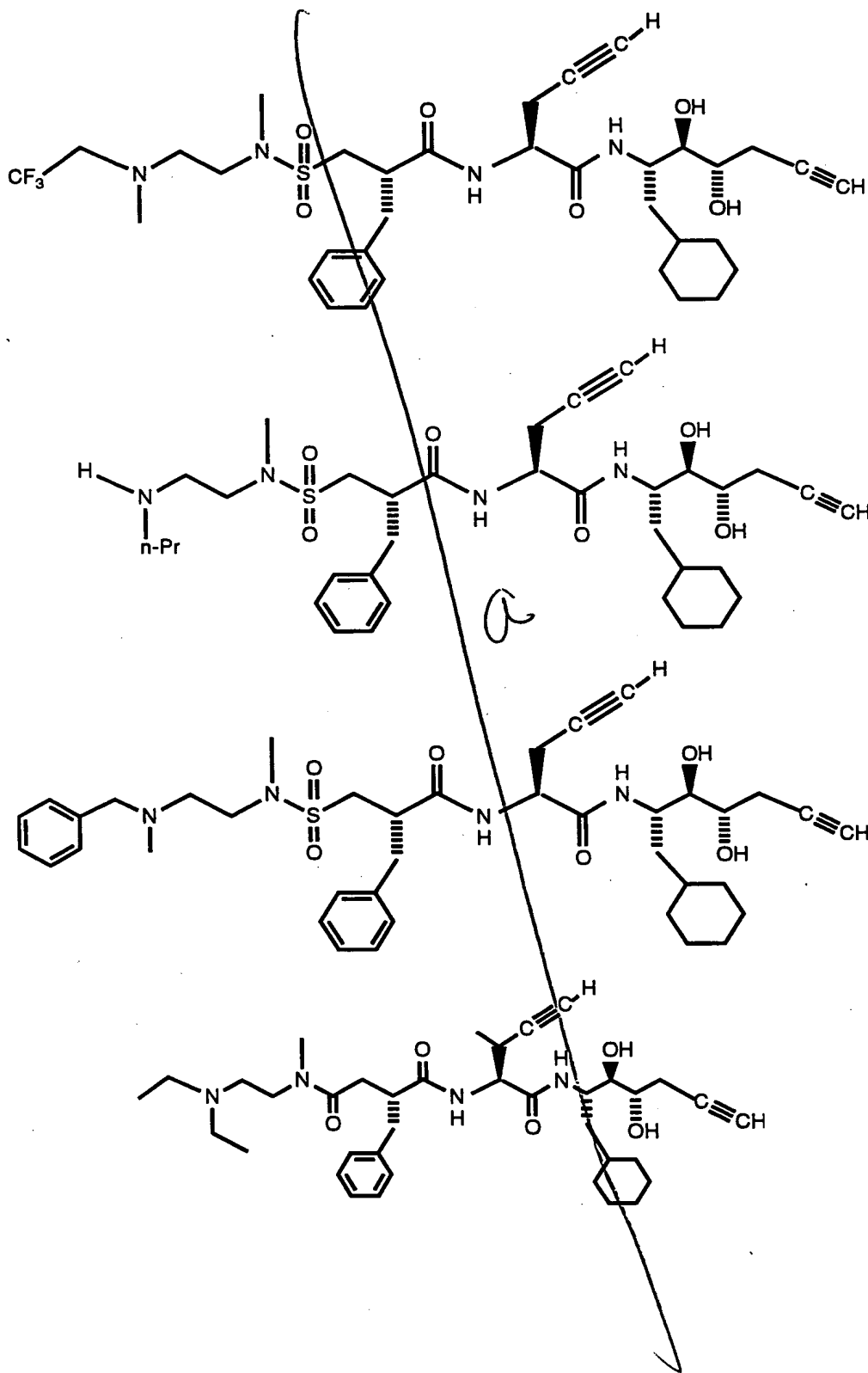
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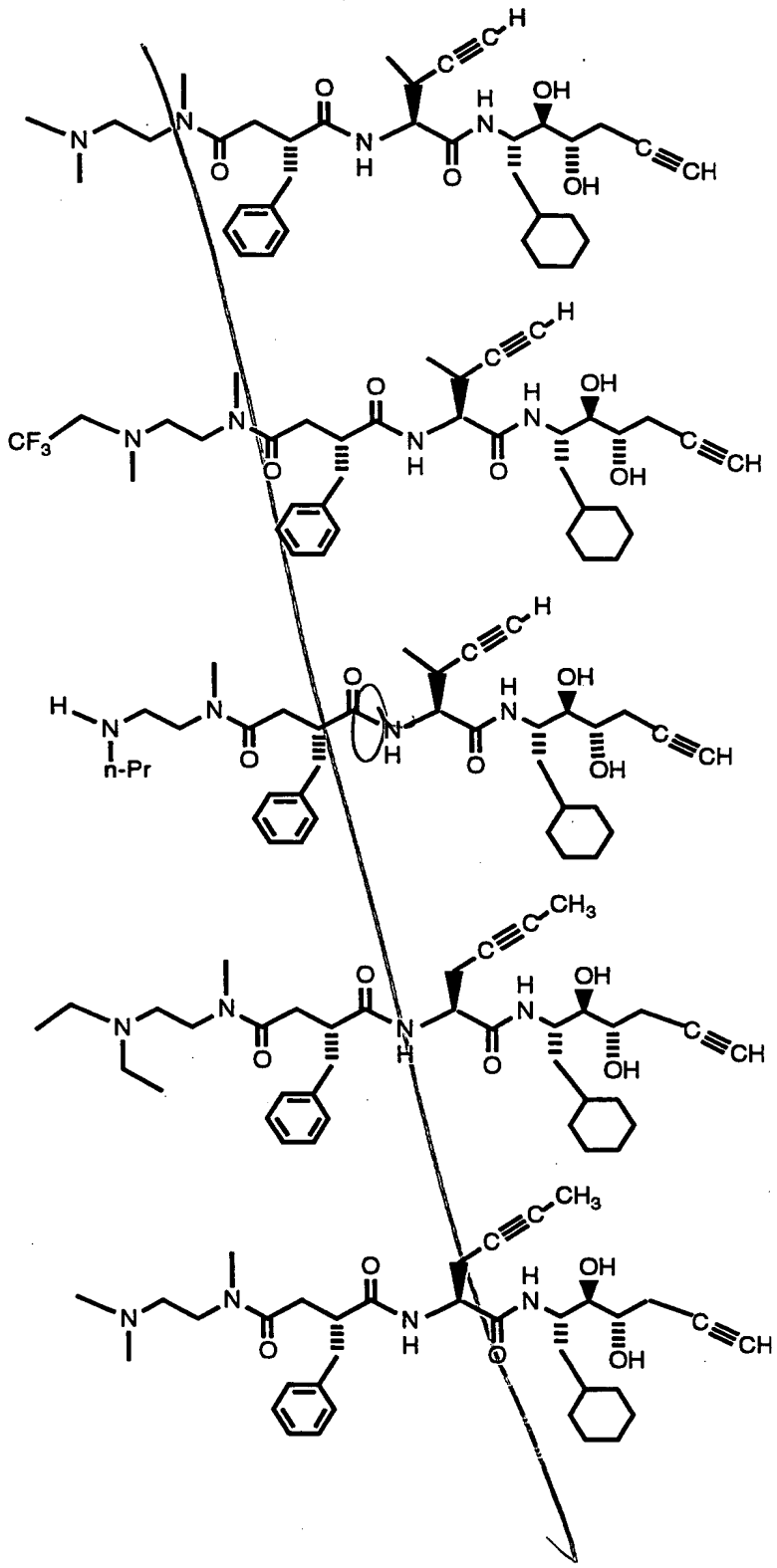


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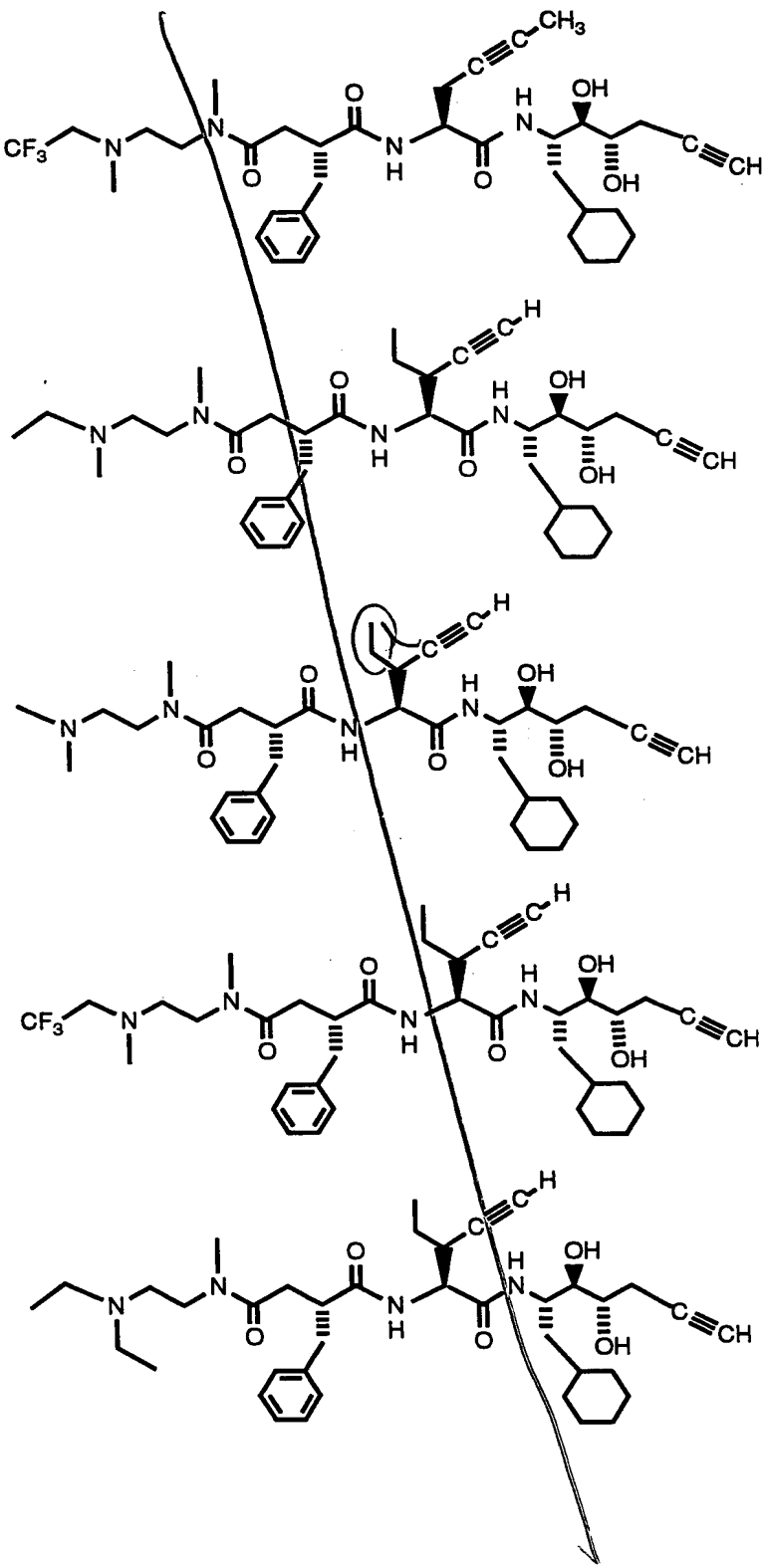
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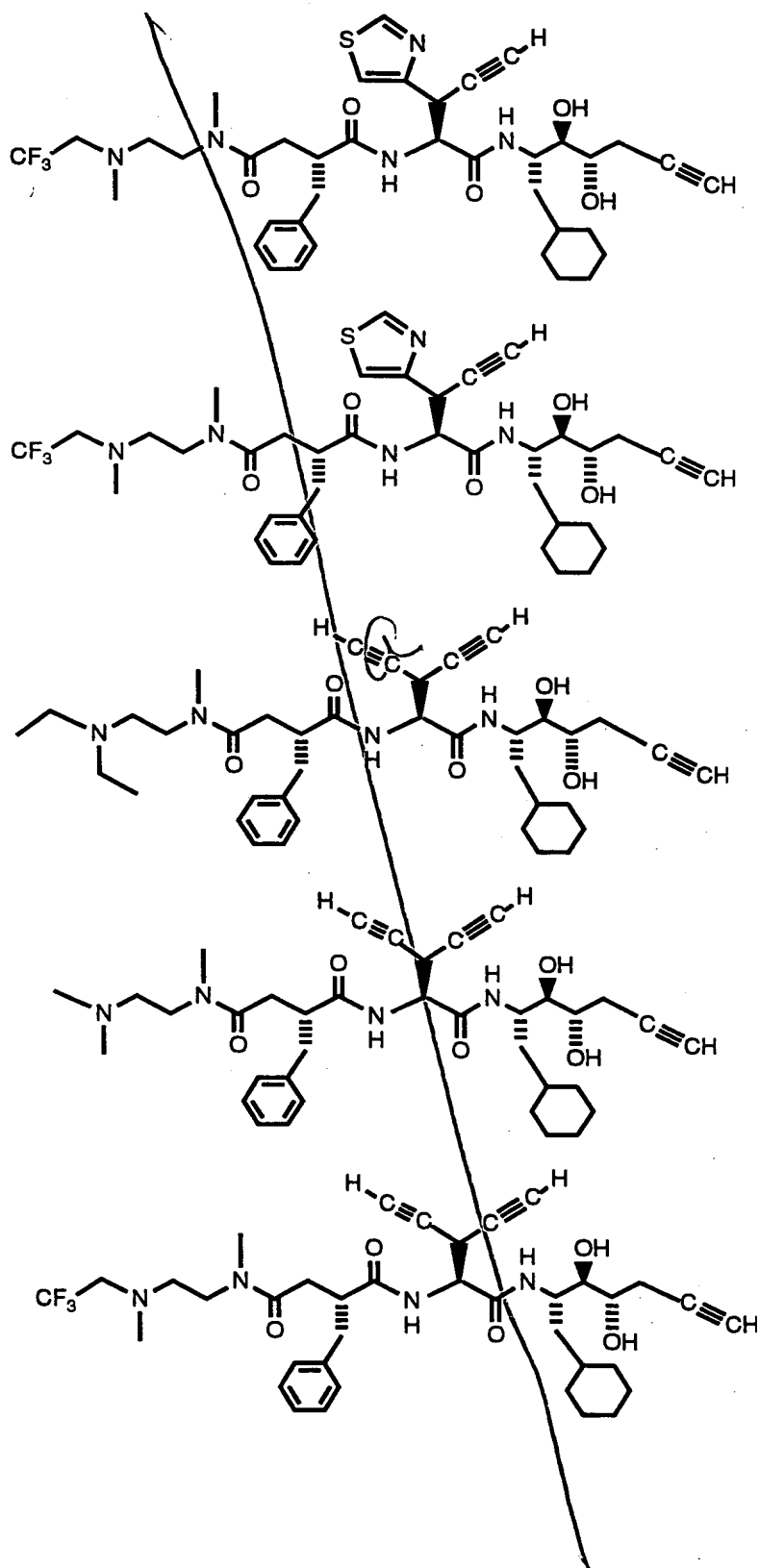
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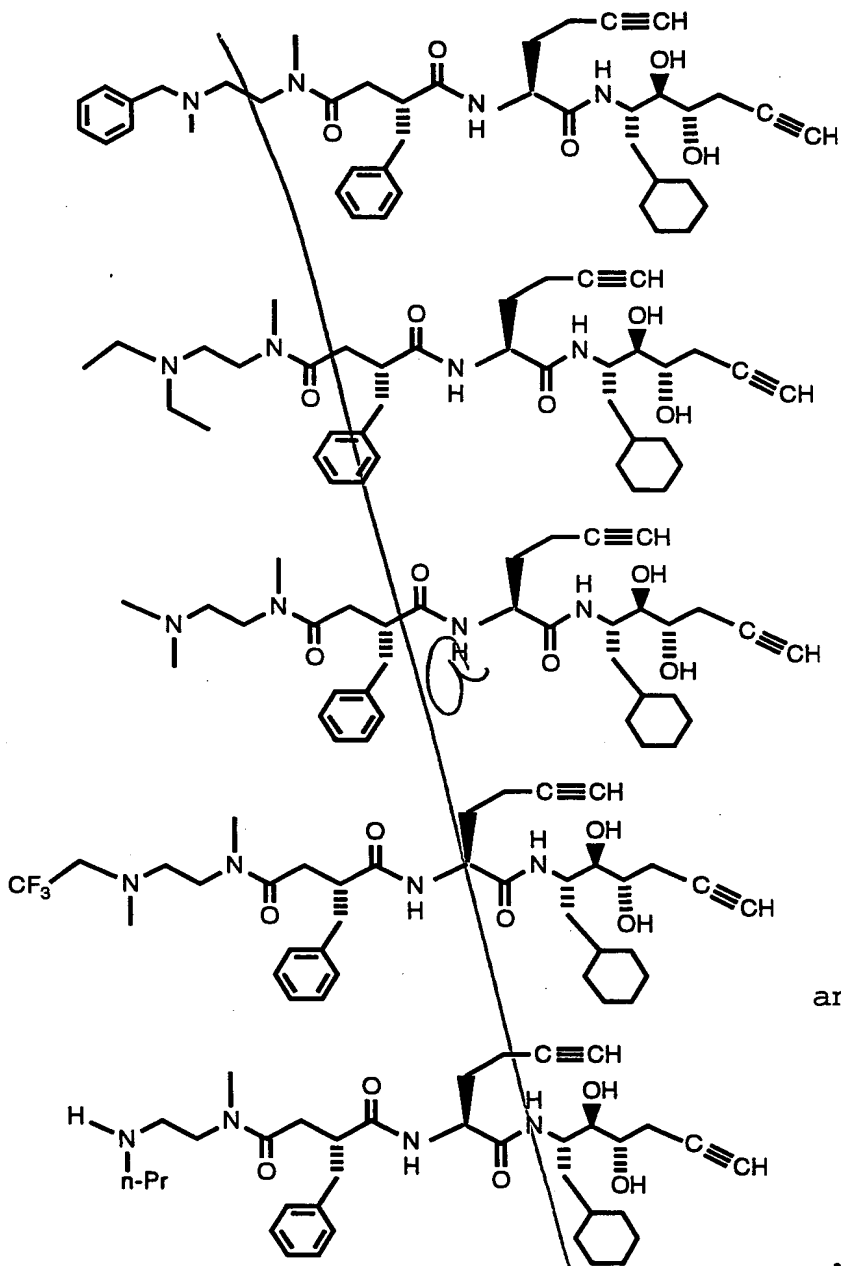
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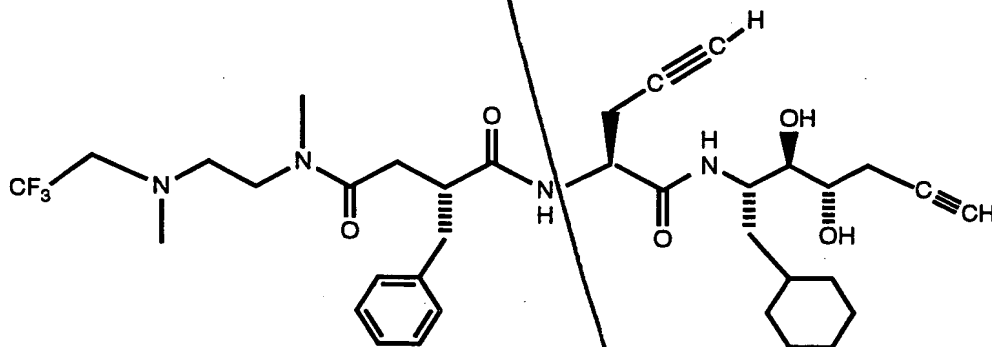
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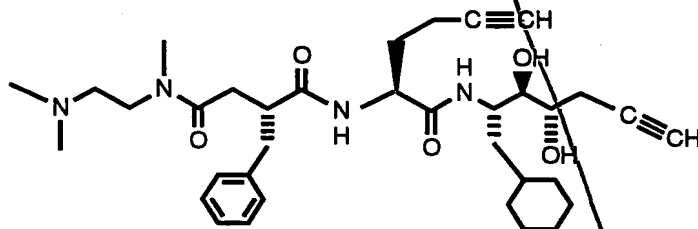
19. The composition of Claim 17 wherein said renin-inhibiting compound is N1-[1R*-[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-hexynyl]amino]carbonyl]-3-butynyl]-N4-[2-(dimethylamino)ethyl]-N4-methyl-2S*-(phenylmethyl)butanediamide or a pharmaceutically-acceptable salt thereof.

20. The composition of Claim 17 wherein said renin-inhibiting compound is [1R*-[[[1R*-[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-hexynyl]amino]carbonyl]-3-butynyl]amino]carbonyl]-2-phenylethyl][2-(dimethylamino)ethyl]methylcarbamate or a pharmaceutically-acceptable salt thereof.

21. The composition of Claim 17 wherein said renin-inhibiting compound is



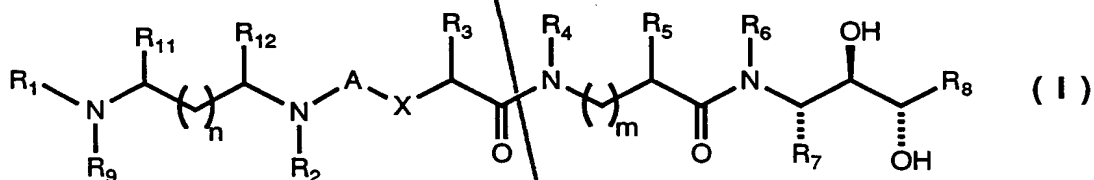
22. The composition of Claim 17 wherein said renin-inhibiting compound is



or a pharmaceutically-acceptable salt thereof.

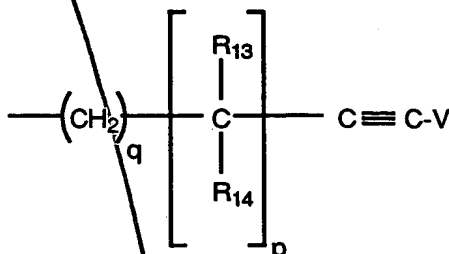
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23. A therapeutic method for treating a circulatory disorder or a circulatory-related disorder, said method comprising administering to a subject susceptible to or afflicted with such disorder a therapeutically-effective amount of an active compound of Formula I:



wherein A is selected from methylene, CO, SO and SO₂;
 wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido, alkyl and benzyl;
 wherein each of R₁ and R₉ is a group independently selected from hydrido, alkyl, cycloalkyl, alkoxyacyl, haloalkyl, alkoxycarbonyl, benzyloxycarbonyl, loweralkanoyl, haloalkylacyl, phenyl, benzyl, naphthyl, and naphthylmethyl, any one of which groups having a substitutable position may be optionally substituted with one or more radicals selected from alkyl, alkoxy, alkenyl, alkynyl, halo, haloalkyl, cyano and phenyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide;
 wherein R₂ is selected from hydrido, alkyl, dialkylaminoalkyl, alkylacylaminoalkyl, benzyl and cycloalkyl; wherein R₃ is selected from alkyl, cycloalkylalkyl, acylaminoalkyl, phenylalkyl, naphthylmethyl, aryl, heterocyclicalkyl and heterocycliccycloalkyl, wherein the cyclic portion of any of said phenylalkyl, naphthylmethyl, aryl, heterocyclicalkyl and heterocycliccycloalkyl groups may be substituted by one or more radicals selected from halo, hydroxy, alkoxy and alkyl; wherein each of R₄ and R₆ is independently selected from hydrido, alkyl, benzyl

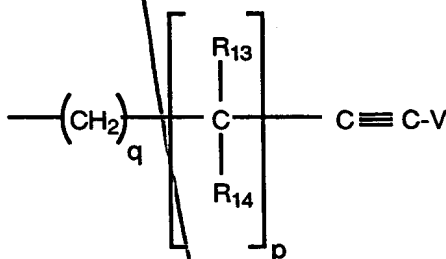
and cycloalkyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl, cycloalkyl, haloalkyl, benzyl and phenyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, phenyl, heterocyclic, heterocyclicalkyl and heterocycliccycloalkyl; wherein R₇ is selected from substituted or unsubstituted alkyl, cycloalkyl, phenyl, cycloalkylalkyl and phenylalkyl, any one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo, haloalkyl, alkenyl, alkynyl and cyano; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, haloalkyl, dialkylamino and phenyl; and wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

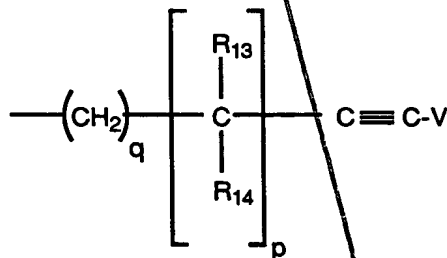
24. The method of Claim 23 wherein A is selected from methylene, CO, SO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido, alkyl and benzyl; wherein each of R₁ and R₉ is independently selected from hydrido, lower alkyl, haloalkyl, cycloalkyl, alkoxycarbonyl, benzyloxycarbonyl, loweralkanoyl, alkoxyacyl, phenyl and benzyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an

N-oxide; wherein each of R₂, R₄ and R₆ is independently selected from hydrido and alkyl; wherein R₃ is selected from phenylalkyl, naphthylmethyl, cyclohexylalkyl, cyclopentylalkyl, heteroarylalkyl and
 5 heteroarylcycloalkyl; wherein each of R₅ and R₈ is independently selected from



10 wherein V is selected from hydrido, alkyl, haloalkyl, benzyl and phenyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, heteroarylalkyl and heteroarylcycloalkyl; wherein R₇ is
 15 selected from substituted or unsubstituted cyclohexylmethyl and benzyl, either one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo and haloalkyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl,
 20 dialkylamino and phenyl; wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

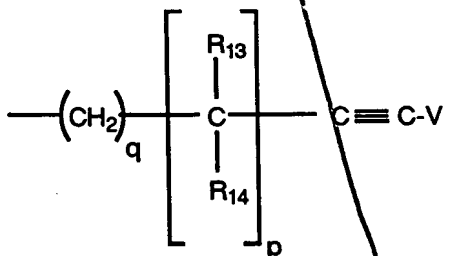
25. The method of Claim 24 wherein A is selected from methylene, CO, SO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido, alkyl and benzyl; wherein each of R₁ and R₉ is independently selected from hydrido, alkyl, alkoxyacyl, haloalkyl, alkoxycarbonyl, benzyloxycarbonyl and benzyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein each of R₂, R₄ and R₆ is independently selected from hydrido and alkyl; wherein R₃ is selected from benzyl, phenethyl, cyclohexylmethyl, phenpropyl, pyrrolidinyl, piperidinyl, pyrrolidinylmethyl, piperidinylmethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl and haloalkyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, thiazole and thiazolemethyl; wherein R₇ is cyclohexylmethyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero

through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

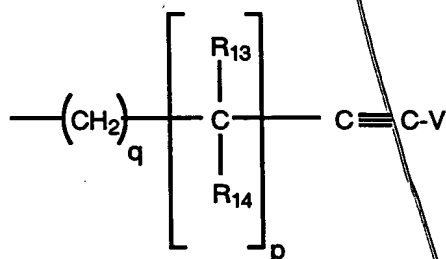
- 5 26. The method of Claim/25 wherein A is selected from CO and SO₂; wherein X is selected from oxygen atom, methylene and >NR_{10} with R₁₀ selected from hydrido and methyl; wherein each of R₁ and R₉ is independently selected from hydrido, lower alkyl, alkoxyacyl, alkoxy carbonyl, benzyloxycarbonyl, haloalkyl and benzyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, phenethyl, cyclohexylmethyl, pyrrolidinyl, piperidinyl, pyrrolidinylmethyl, piperidinylmethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₅ and R₈ is independently selected from



- wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, alkyl and alkynyl; wherein R₇ is cyclohexylmethyl; wherein each of

R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

27. The method of Claim 26 wherein A is selected from CO and SO₂; wherein X is selected from oxygen atom and methylene; wherein each of R₁ and R₉ is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, cyclohexylmethyl, phenethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R₅ and R₈ is independently selected from



wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, methyl, ethyl, propyl and ethynyl; wherein R₇ is

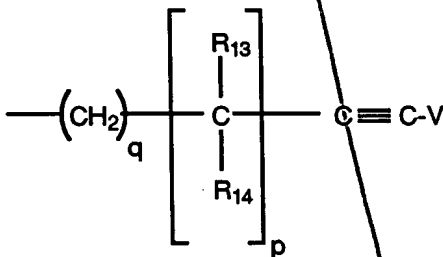
cyclohexylmethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

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28. The method of Claim 27 wherein A is selected from CO and SO₂; wherein X is selected from oxygen atom and methylene; wherein each of R₁ and R₉ is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, cyclohexylmethyl, phenethyl, imidazolemethyl, pyridylmethyl and 2-pyridylethyl; wherein each of R₅ and R₈ is independently selected from

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wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R₁₃ and R₁₄ is a radical independently selected from hydrido, methyl and ethynyl; wherein R₇ is cyclohexylmethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl and phenyl; wherein m is

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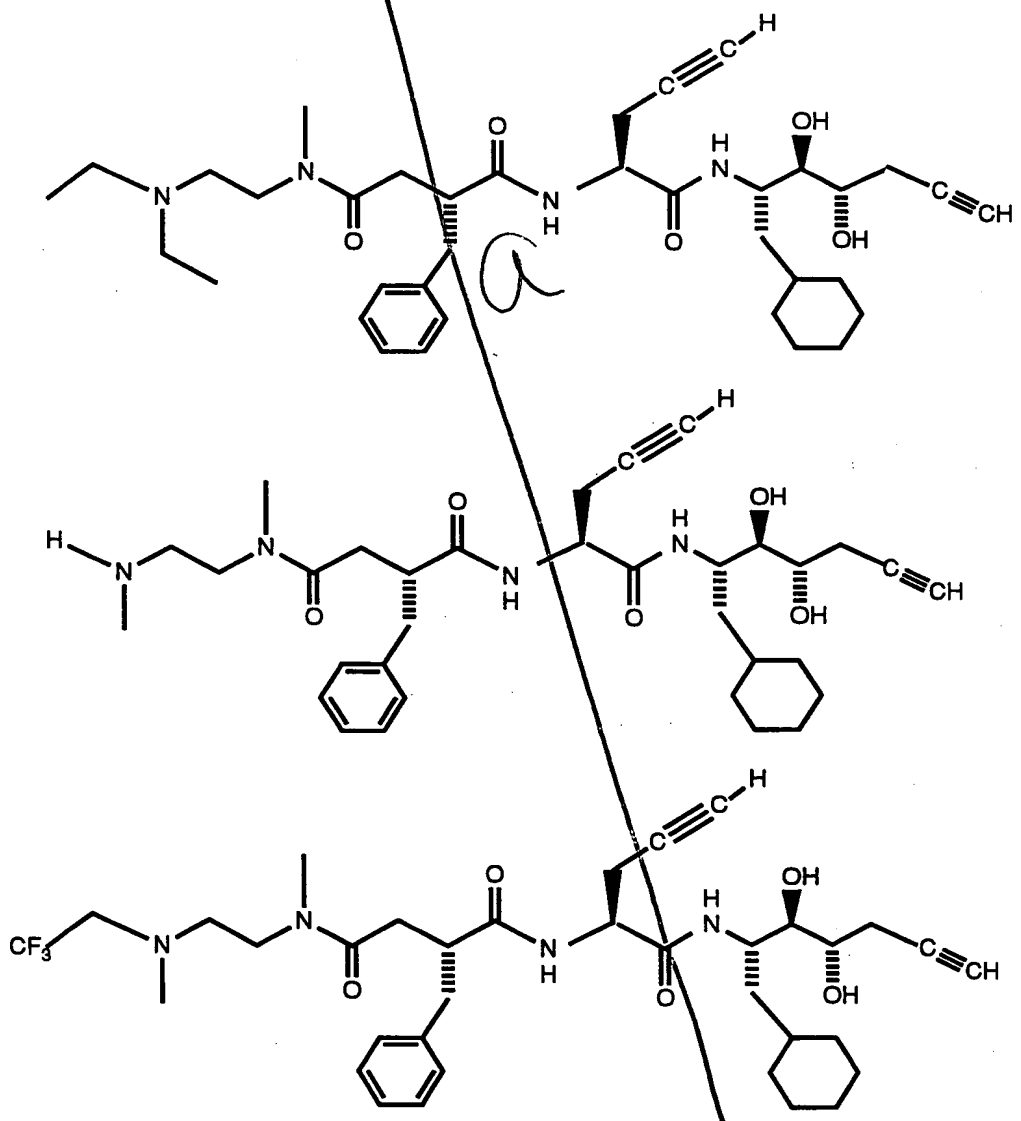
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zero; wherein n is a number selected from zero through three; wherein p is a number selected from one through three; and wherein q is zero or one; or a pharmaceutically-acceptable salt thereof.

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29. The method of Claim 28 wherein said compound is selected from compounds, their tautomers, and the pharmaceutically-acceptable esters and salts thereof, of the group consisting of

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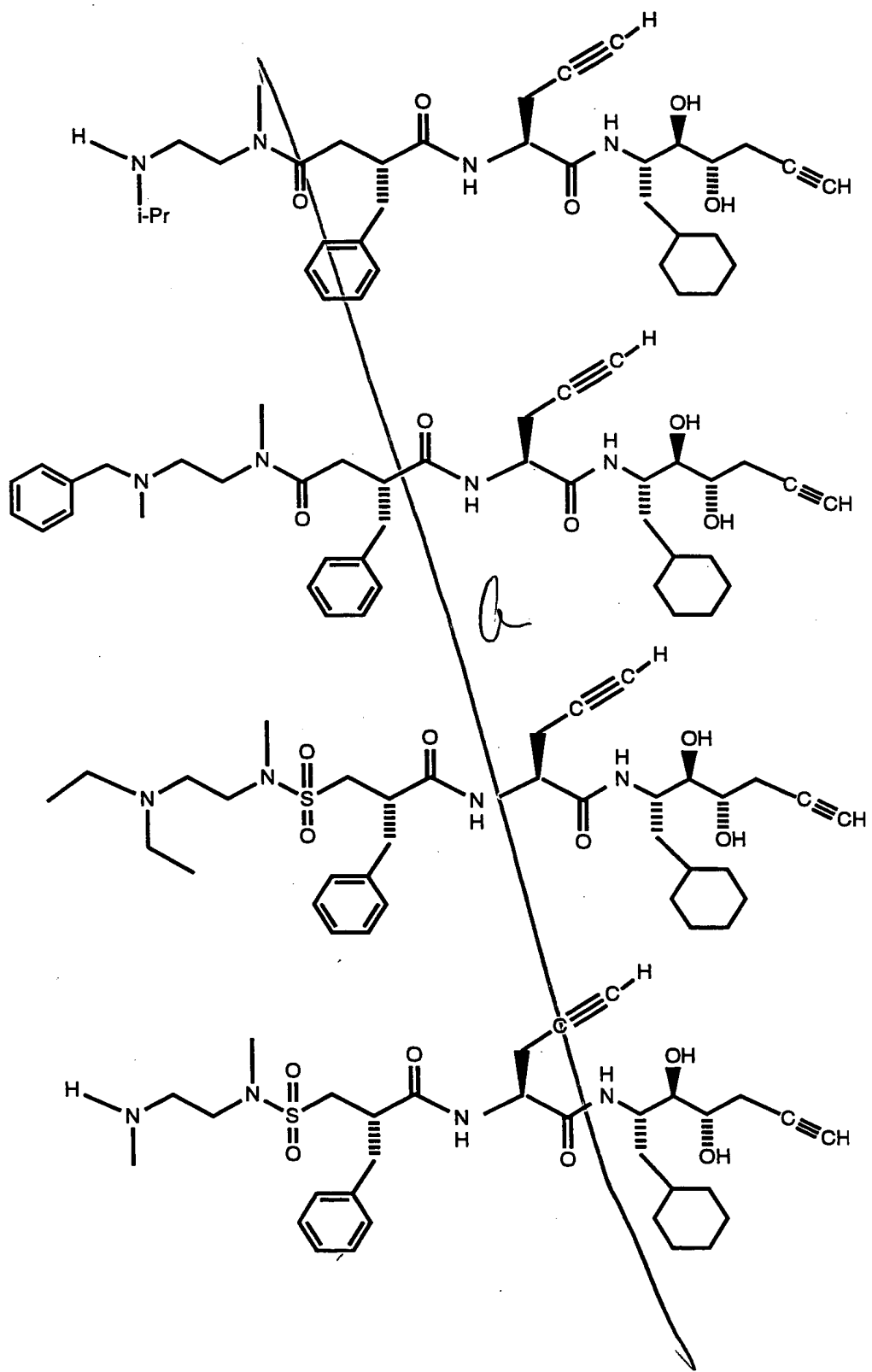


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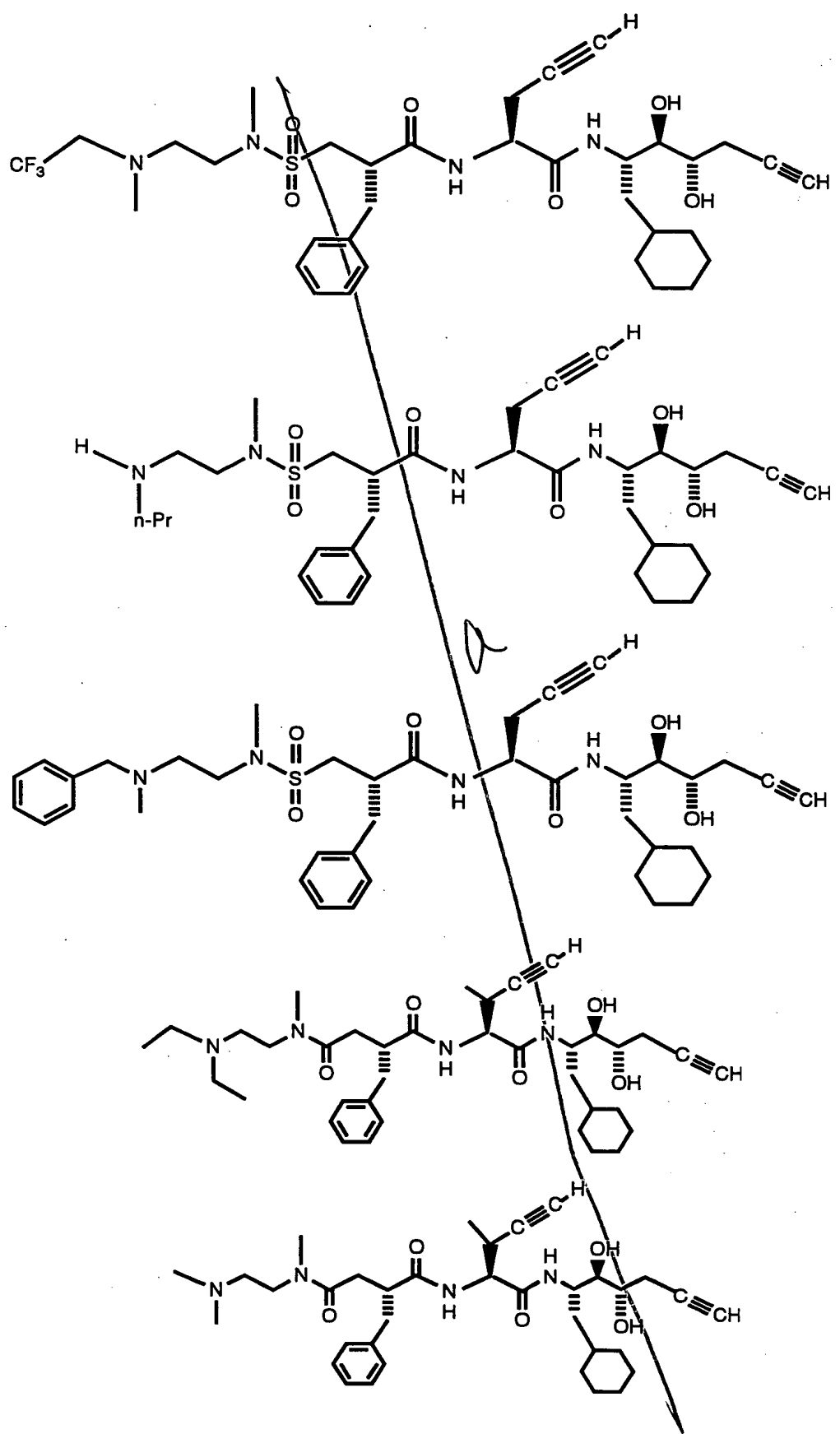
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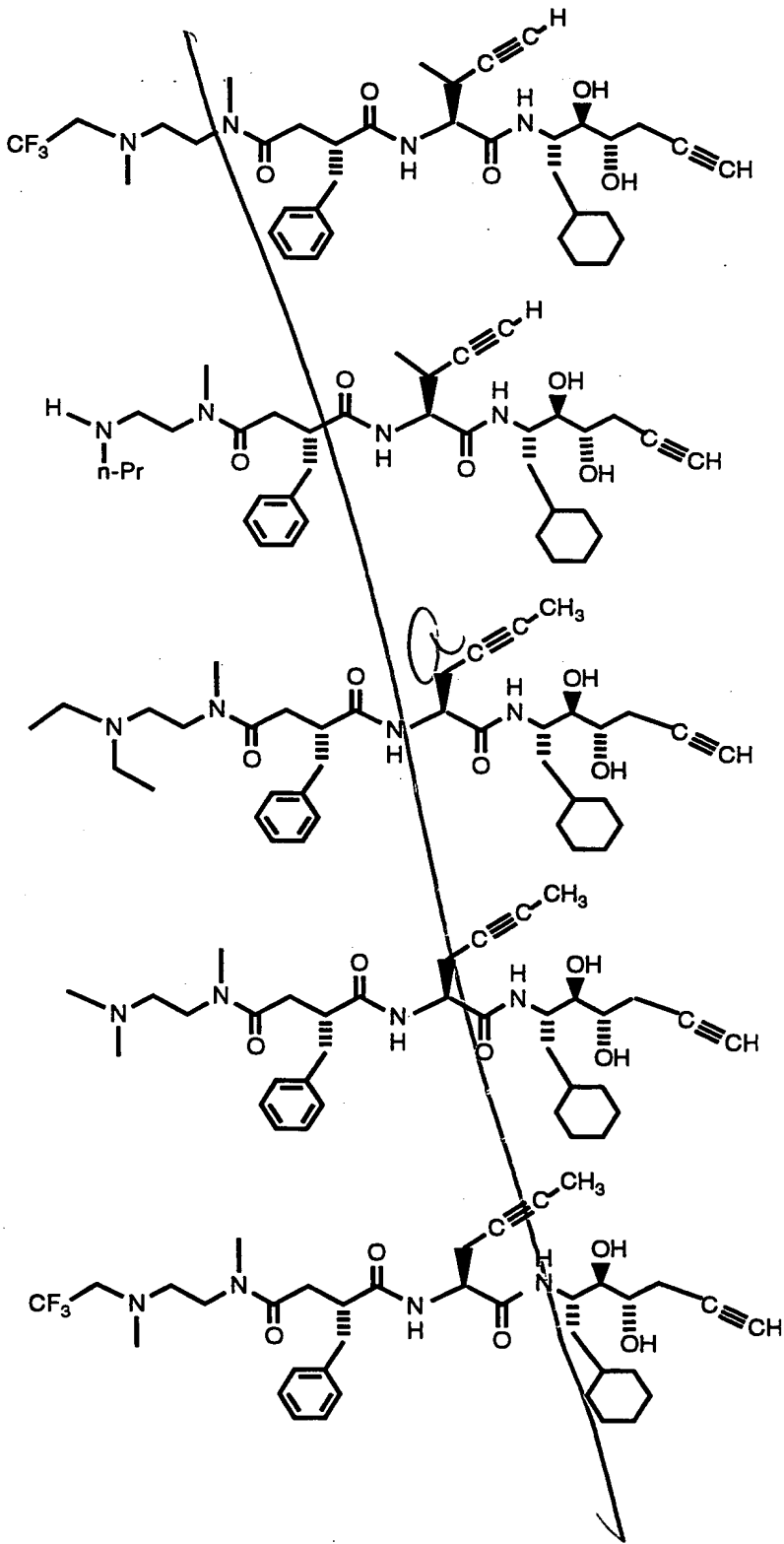
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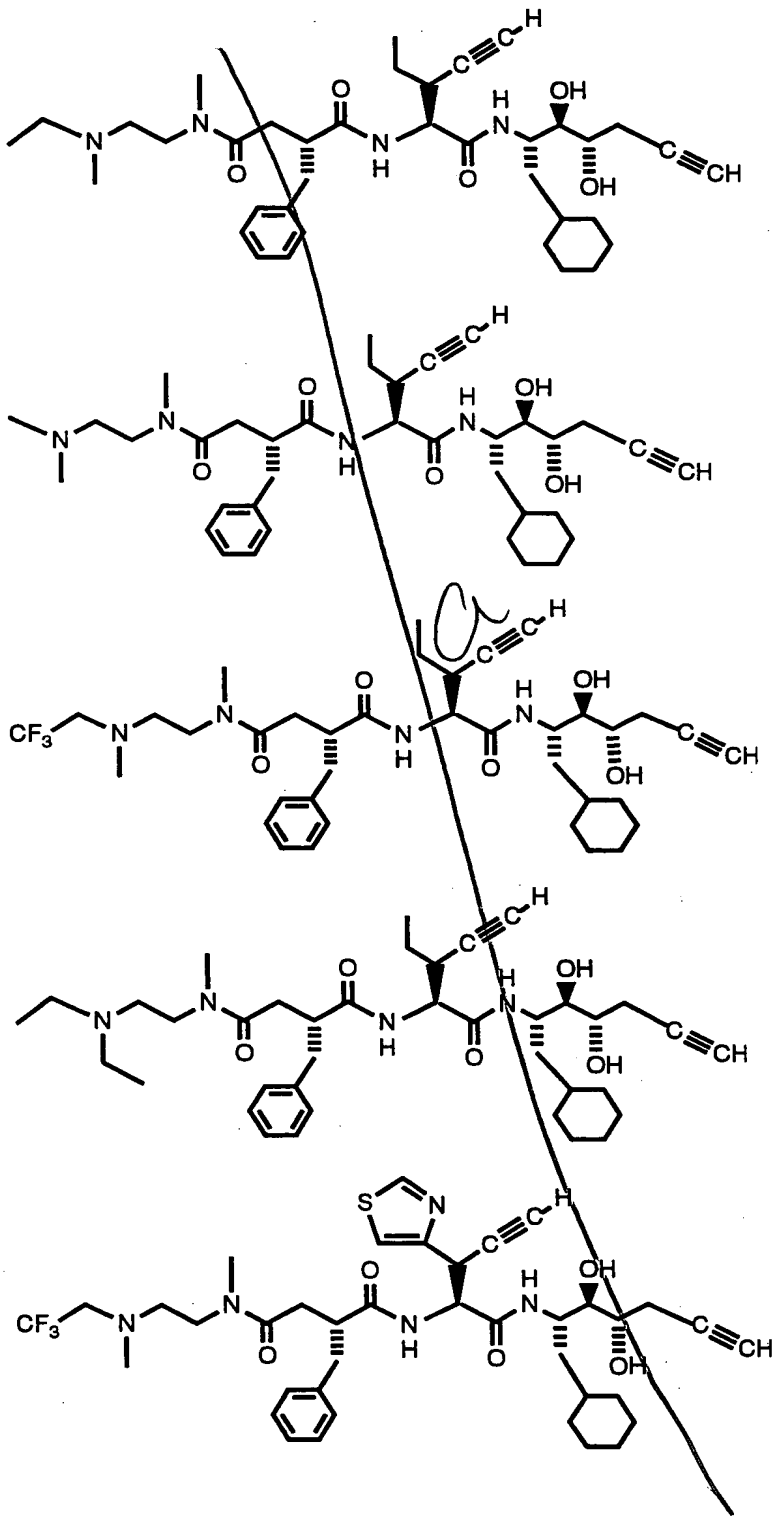


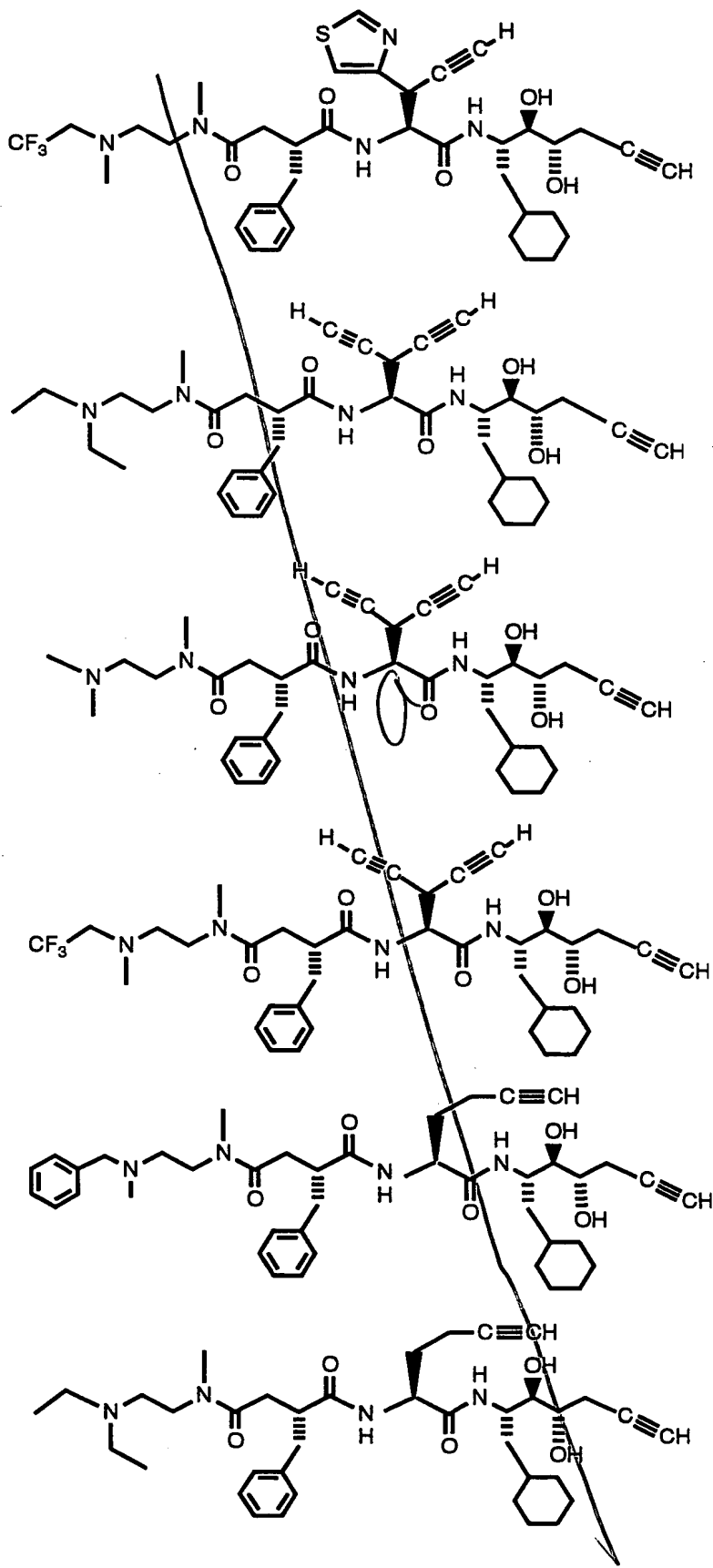
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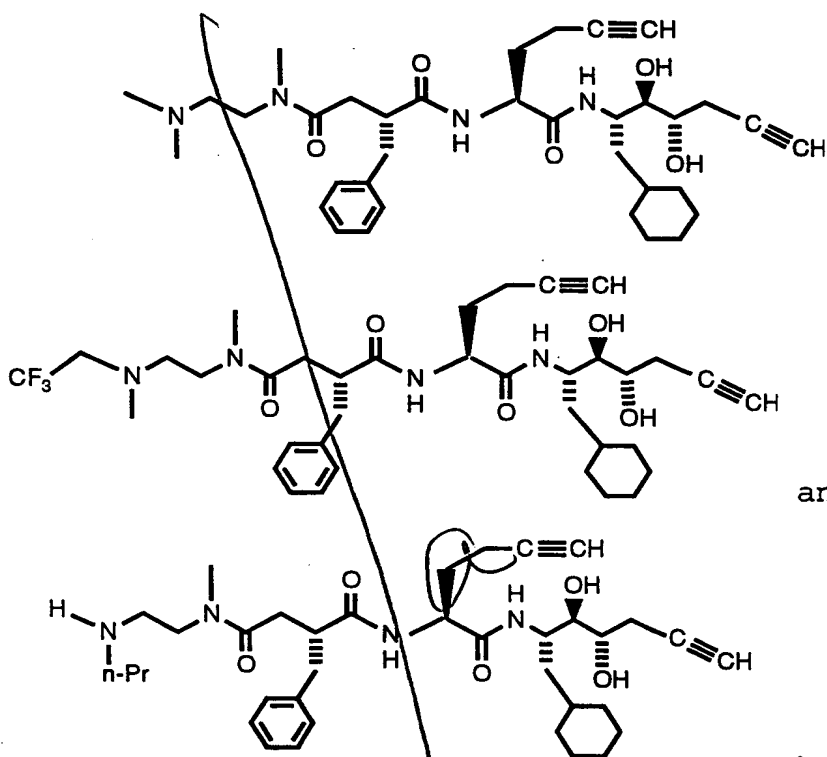




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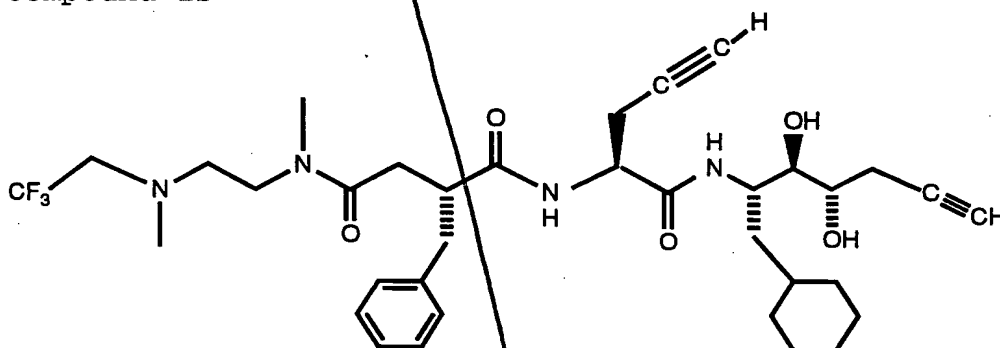


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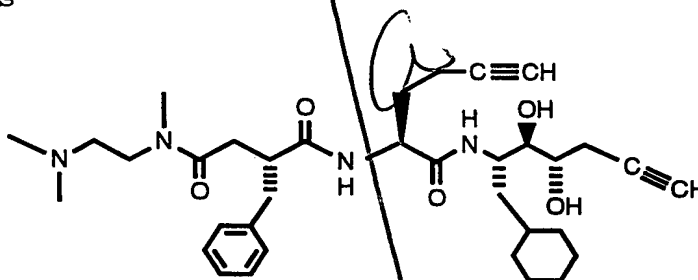
30. The method of Claim 28 wherein said compound is N1-[1R*-[[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-hexynyl]amino]carbonyl]-3-butynyl]-N4-[2-(dimethylamino)ethyl]-N4-methyl-2S*-(phenylmethyl)butanediamide or a pharmaceutically-acceptable salt thereof.

31. The method of Claim 28 wherein said compound is [1R*-[[[[1R*-[[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-hexynyl]amino]carbonyl]-3-butynyl]amino]carbonyl]-2-phenylethyl][2-(dimethylamino)ethyl]methylcarbamate or a pharmaceutically-acceptable salt thereof.

32. The method of Claim 28 wherein said compound is



33. The method of Claim 28 wherein said compound is



or a pharmaceutically-acceptable salt thereof.

34. The method of Claim 23 wherein said circulatory disorder is a cardiovascular disorder.

35. The method of Claim 34 wherein said cardiovascular disorder is hypertension.

36. The method of Claim 23 wherein said circulatory-related disorder is glaucoma.

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